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(54) Title: INDGLINONE COMBINATORIAL LIBRARIES AND RELATED PRODUCTS AND METHODS FOR THE TREATMENT OF DISEASE

(57) Abstract

The present invention relates to organic molecules capable of modulating, regulating and/or inhibiting protein kinase signal transduction. Such compounds are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis and restenosis and metabolic diseases such as diabetes. The present invention features indolinone compounds that potently inhibit protein kinases and related products and methods. Inhibitors specific to the FLK protein kinase can be obtained byadding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone, in particular at the 1' position of the indole ring. Indolinone compounds that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano-b-pyrrol moiety. Indolinone compounds that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosoluble indolinone compounds that are tyrosine kinase inhibitors and related products and methods.

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1

DESCRIPTION

Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease

Introduction

The present invention relates to novel compounds capable of modulating, regulating and/or inhibiting protein kinase signal transduction. The present invention is also directed to methods of regulating, modulating or inhibiting protein kinases, whether of the receptor or non-receptor class, for the prevention and/or treatment of disorders related to unregulated protein kinase signal transduction, including cell proliferative and metabolic disorders.

Background of the Invention

The following description of the background of the invention is provided to aid in understanding the invention, but is not admitted to be or describe prior art to the invention.

Protein kinases and protein phosphatases regulate a wide variety of cellular processes including metabolism, cell proliferation, cell differentiation, and cell survival by participating in signal transduction pathways.

Alterations in the cellular function of a protein kinase or protein phosphatase can give rise to various diseased states in an organism. For example, many types of cancer tumors are associated with increases in the activity of specific protein kinases. Cell and tissue degeneration can also be associated with decreases in the activity of particular protein kinases.

Cellular signal transduction is a fundamental mechanism whereby extracellular stimuli are relayed to the interior of cells. One of the key biochemical mechanisms

2

of signal transduction involves the reversible phosphorylation of proteins. Phosphorylation of amino acids regulates the activity of mature proteins by altering their structure and function.

Phosphate most often resides on the hydroxyl moiety of serine, threonine, or tyrosine amino acids in proteins. Enzymes that mediate phosphorylation of cellular effectors fall into two classes. While protein phosphatases hydrolyze phosphate moieties from phosphoryl protein substrates, protein kinases transfer a phosphate moiety from adenosine triphosphate to protein substrates. The converse functions of protein kinases and protein phosphatases balance and regulate the flow of signals in signal transduction processes.

Protein kinases are divided into two groups - receptor and non-receptor type proteins. Receptor protein kinases comprise an extracellular region, a transmembrane region, and an intracellular region. Part of the intracellular region of receptor protein kinases harbors a catalytic domain. While non-receptor protein kinases do not harbor extracellular or transmembrane regions, they do comprise a region similar to the intracellular regions of their receptor counterparts.

Protein kinases are divided further into three classes based upon the amino acids they act upon. Some incorporate phosphate on serine or threonine only, some incorporate phosphate on tyrosine only, and some incorporate phosphate on serine, threonine, and tyrosine.

In an effort to discover novel treatments for dis-30 eases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein kinases. Some small organic molecules form a class of compounds that modulate the function of protein kinases.

3

The compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein kinase inhibitors only weakly inhibit the function of protein kinases. In addition, many inhibit a variety of protein kinases and will therefore cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules that potently inhibit only specific protein kinases. Indolinone synthesis, methods of testing the biological activity of indolinones, and inhibition patterns of some indolinone derivatives are described in International Patent Publication No. WO96/40116, published December 19, 1996 entitled "Benzylidene-Z-Indolinone Compounds for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 223/298) and International Patent Publication No. WO 96/22976, published August 1, 1996 by Ballinari et al., both of which are incorporated herein by reference in their entirety, including any drawings.

Despite the significant progress that has been made in developing indolinone based pharmaceuticals, there 25 remains a need in the art to identify the particular structures and substitution patterns that cause inhibition of particular protein kinases and other specified biological activities.

30 Summary of The Invention

The present invention relates to organic molecules capable of modulating, regulating and/or inhibiting protein kinase signal transduction. Such compounds are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell

4

proliferative diseases such as cancer, atherosclerosis, arthritis and restenosis and metabolic diseases such as diabetes. The protein kinases effected include, but are not limited to Flk, FGFR, PDGFR, and raf.

5 The present invention features indolinone compounds that potently inhibit protein kinases and related products Inhibitors specific to the FLK protein and methods. kinase can be obtained by adding chemical substituents to the 3-[(indole-3-yl)methylene]-2-indolinone, in particular 10 at the 1' position of the indole ring. Indolinone compounds that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano-b-pyrrol moiety. Indolinone compounds that are modified with substituents, 15 particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosoluble indolinone compounds that are tyrosine kinase inhibitors and related products and methods.

The compounds of the invention represent a new generation of potential therapeutics for diseases caused by one or more non-functional protein kinases. Neuro-degenerative diseases fall into this class of diseases, including, but not limited to Parkinson's Disease and Alzheimers disease. The compounds can be modified such that they are specific to their target or targets and will subsequently cause few side effects and thus represent a new generation of potential cancer therapeutics. These properties are significant improvements over the currently utilized cancer therapeutics that cause multiple side effects and deleteriously weaken patients.

It is believed the compounds of the invention will minimize and obliterate solid tumors by specifically inhibiting the activity of the FLK protein kinase, or will

5

at least modulate or inhibit tumor growth and/or metastases. The FLK protein kinase regulates proliferation of blood vessels during angiogenesis. Increased rates of angiogenesis accompany cancer tumor growth in cells as cancer tumors must be nourished by oxygenated blood during growth. Therefore, inhibition of the FLK protein kinase and the corresponding decreases in angiogenesis will starve tumors of nutrients and most likely obliterate them.

10 While a precise understanding of the mechanism by which compounds inhibit PTKs (e.g., the fibroblast growth factor receptor 1 [FGFR1]) is not required in order to practice the present invention, the compounds are believed to interact with the amino acids of the PTKs' catalytic region. PTKs typically possess a bi-lobate structure, and ATP appears to bind in the cleft between the two lobes in a region where the amino acids are conserved among PTKs; inhibitors of PTKs are believed to bind to the PTKs through non-covalent interactions such as hydrogen bonding, Van der Waals interactions, and ionic bonding, in the same general region that ATP binds to the PTKs. specifically, it is thought that the oxindole component of the compounds of the present invention binds in the same general space occupied by the adenine ring of ATP. Specificity of an indolinone PTK inhibitor for a particular PTK may be conferred by interactions between the constituents around the oxindole core with amino acid domains specific to individual PTKs. Thus, different indolinone substitutents may contribute to preferential binding to particular PTKs. binding to particular PTKs. The ability to select those (or other nucleotide) compounds active at different ATP binding sites makes them useful in targeting any protein with such a site, not only

protein tyrosine kinases, but also serine/threonine kinases and protein phosphatases. Thus, such compounds

6

have utility for *in vitro* assays on such proteins and for *in vivo* therapeutic effect through such proteins.

In one aspect the invention features a combinatorial library of indolinone compounds. The library includes a 5 series of at least ten (preferably at least 50-100, more preferably at least 100-500, and most preferably at least 500-5,000) indolinones that can be formed by reacting an oxindole compound with an aldehyde. In preferred embodiments the indolinones in the library can be formed by 10 reacting a type A oxindole with a type B aldehyde. Type A oxindoles and type B aldehydes are shown in Figures 1 and 2 respectively (and Tables 11 and 12 respectively), as explained in detail below. As can be seen, in the figures the oxindoles are labeled 01, 02, 03, ... and the alde-15 hydes are named A1, A2, A3, Thus, one can readily appreciate that the combinatorial library could include any and all combinations of oxindoles and aldehydes, including the indolinones resulting from 01 and A1, 01 and A2, 01 and A3, 02 and A1, 02 and A2, 02 and A3, 03 and A1, 20 03 and A2, 03 and A3 and so on. Similarly, the indolinones in the library can be formed by any combination of the oxindoles in Table 11 with any of the aldehydes listed in Figure 2 or Table 12. Finally, the indolinones may also, of course, come from any combination 25 of aldehydes listed in Table 12 with any oxindoles from Figure 1 or Table 11.

The term "combinatorial library" refers to a series of compounds. In the present case, the combinatorial library contains a series of indolinone compounds that can be formed by reacting an oxindole and an aldehyde. A wide variety of oxindoles and aldehydes may be used to create the library of indolinones.

The term "indolinone" is used as that term is commonly understood in the art and includes a large subclass

7

of substituted or unsubstituted compounds that are capable of being synthesized from an aldehyde moiety and an oxindol moiety, such as the compounds shown below.

The term "type A oxindole" is meant to include any and all of the oxindoles set forth in Figure 1 and Table 11. Oxindoles, as that term is used herein, typically have the structure set forth below:

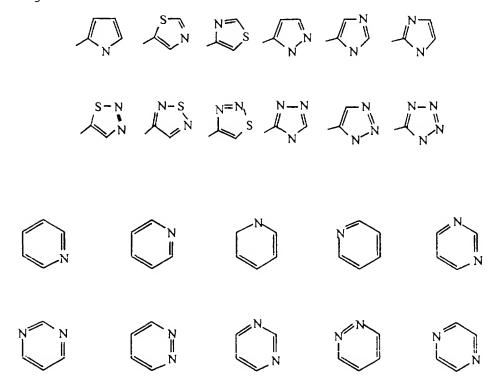
(I)

10 wherein,

- (a) A_1 , A_2 , A_3 , and A_4 are independently carbon or nitrogen;
 - (b) R₁ is hydrogen or alkyl;
 - (c) R₂ is oxygen or sulfur;
- 15 (d) R₃ is hydrogen;
- (e) R₄, R₅, R₆, and R₇ (i) are each independently selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R, and CONRR' or (ii) any two adjacent R₄, R₅, R₆, and R₇ taken together form a fused ring with the aryl portion of the oxindole-based portion of the indolinone.

It is to be understood that when A_1 , A_2 , A_3 , and A_4 is nitrogen or sulfur that the corresponding R_4 , R_5 , R_6 , or R_7 is nothing and that the corresponding bond shown in structure I does not exist.

Examples of oxindoles having such fused rings (as described in (e) (ii) above) are shown in Fig. 1, compounds 044, 045, 047, 048, 050, 051, 052, 053, 055, 056, 058, 059, 061, 062, 064, 066, 067, 069, 070, and 073. Other examples of suitable fused rings include the following:



The six membered rings shown above also exemplify possible A rings in the structures II, III and IV.

The term "type B aldehyde" includes any and all of the aldehydes set forth in Figure 2 and Table 11. The term "aldehyde" is used as is commonly understood in the art to include substituted and unsubstituted aldehydes of the structure R_d CHO where R_d can be a wide variety of substituted or unsubstituted groups such as alkyl and aryl.

In yet another aspect, the invention provides a method of synthesizing an indolinone by reacting a type A oxindole with a type B aldehyde. The method of making the indolinones of the present invention may involve creating a combinatorial library of compounds as described above, testing each compound in biological assays such as those described herein, selecting one or more suitable compounds and synthesizing the selected compound or compounds.

Also featured is an indolinone compound having 10 formula II or III:

$$\begin{array}{c|c} R_{3}' & R_{4}' \\ R_{2}' & R_{5}' \\ R_{5} & R_{6}' \\ R_{7} & R_{1} \\ \end{array}$$

(II)

(III)

wherein:

- (a) A_1 , A_2 , A_3 , and A_4 are independently carbon or nitrogen;
 - (b) R, is hydrogen or alkyl;
 - (c) R, is oxygen or sulfur;
 - (d) R₃ is hydrogen;
- (e) R_4 , R_5 , R_6 , and R_7 (i) are each independently selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, $S(\bar{O})R$, SO_2NRR' , SO_3R , SR, NO_2 , NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, $(CH_2)_nCO_2R$, and CONRR' or (ii) any two adjacent R_4 , R_5 , R_6 , and R_7 taken together form a fused ring with the aryl ring of the oxindole-based portion of the indolinone;
- (f) R₂', R₃', R₄', R₅', and R₆' are each independently selected from the group consisting of hydrogen, alkyl, 20 alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R, and CONRR';
 - (g) n is 0, 1, 2, or 3;
 - (h) R is hydrogen, alkyl or aryl;
- 25 (i) R' is hydrogen, alkyl or aryl; and

(j) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, isoxazole, thiazole, isothiazole, 2-sulfonylfuran, 4-5 alkylfuran, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, option-10 ally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)₀CO₂R or CONRR.

As used herein, the term "compound" is intended to include pharmaceutically acceptable salts, esters, amides, prodrugs, isomers and metabolites of the base compound.

In preferred embodiments of structure III, the A substituent may be a five membered heterocycle of formula IV shown below:

D-E \(\) \(

20

(IV)

wherein D, E, F, and G are nitrogen, carbon, or sulfur atoms. The specific juxtaposition of groups D-G is limited to examples of heterocyclic groups known in the chemistry arts, such as the fused rings referred to above and all of which may be optionally substituted as described above in paragraph (j).

In preferred embodiments, the aryl ring ("the A ring") of the oxindole-derived portion of the indolinone (i.e., the ring shown in structures II and III with A_1 , A_2 , A_3 , and A_4) has a polar substituent, preferably selected from the group consisting of NH_2 , COOH, SO_3H , Br, Cl, I, F,

12

COCH₂CH₂COOH, COCH₂Cl, piperazine, and CH₂CH₂NH₂ at the 4, 5, 6, and 7 carbon atom positions (identified by substituents R₄, R₅, R₆, and R₇ respectively in structures V and VI), most preferably hydrophillic groups such as NH₂, COOH, SO₃, COCH₂CH₂COOH, piperazine and CH₂CH₂NH₂.

One approach to choosing target inhibitors of the FGFR (a protein kinase receptor linked to various disorders, such as Pfeiffer, Jackson-Weiss and Cruzon syndromes; dysplasias and hypochondroplasia; dwarfism; bone dysplasia; and developmental disorders involves selecting target compounds with a substituent on the A ring that mimics the triphosphate of ATP and thereby increases the affinity of target compounds for the active-site of the FGFR. Hydrophillic groups may act to mimic the triphosphate at ATP, and also to improve the solubility of the final inhibitor. Without being bound to any theory, it appears that the trans form of the indolinones is generally a more favorable form for FGFR inhibitors.

Amine-based substituents at positions 4, 5, and 6 at 20 the A ring of structures II and III are a preferred class of substituents and an especially preferred class are amines of the structure:

wherein R_a is CO(CH₂)₂COOH, aryl, alkyl, or contains COOH, OH, or NH₂. These types of groups provide steric hindrance in order to force the isomer into a trans conformation which may be a favored property of FGFR inhibition and acts as a linker to a hydrophillic group.

Another favored class of substituents on the aryl 30 ring of structures II and III includes piperazine type substituents of the structure:

WO 98/07695

wherein R_b is preferably a negatively charged group, such as a negatively charged alkyl or acyl.

Yet another preferred class of substituents for the aryl ring of structures II and III are C-COR groups of the formula:

wherein R_c is a hydrophilic or negatively charged group, preferably at the 5 and/or 6 positions of the A ring of structures II and III, such as amide, ester, CH_2CH_2COOH , CH_2Cl , or piperazine. R_c could also be linked to the aryl ring by a sp3 carbon or could be attached as $R_cO_3S_-$.

Yet another preferred set of substituents on the aryl ring are fused heterocyclic rings which can be synthesized by acylation of the arylamine followed by alkylation of the heterocyclic ring systems. Examples of several such compounds are set forth in Figure 1, compounds 044, 045, 047, 048, 050, 051, 052, 053, 055, 056, 058, 059, 061, 062, 064, 066, 067, 069, 070, and 073.

In another aspect, the invention features a 3-[(indole-3-yl)methylene]-2-indolinone compound having a substituent at the 1' position of the indole ring. The substituent at the 1' position of the indole ring is selected from the group consisting of

(a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally

substituted with one or more halogen, or trihalomethyl substituents;

- (b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (c) an aldehyde or ketone of formula -CO-R12, where R12 is selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- 10 (d) a carboxylic acid of formula $-(R_{13})_n$ -COOH or ester of formula $-(R_{14})_m$ -COO- R_{15} , where R_{13} , R_{14} , and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- 15 (e) a sulfone of formula $-(SO_2)-R_{16}$, where R_{16} is selected from the group consisting of alkyl and a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;
- $(f) (R_{17})_n (indole-1-yl) \quad \text{or} \quad (R_{18}) \, m \text{CHOH-} \, (R_{19}) \, p \\ 20 \quad (indole-1-yl), \quad \text{where the indol moiety is optionally} \\ \text{substituted where } R_{17}, \; R_{18}, \; \text{and} \; R_{19} \; \text{are alkyl, and where m,} \\ \text{n, and p are independently 0 or 1; and}$
- (g) taken together with a 2' substituent of the indole ring forms a five or six membered heterocyclic 25 ring.

The term "alkyl" refers to a straight-chain, branched, or cyclic saturated aliphatic hydrocarbon. The alkyl group is preferably 1 to 10 carbons, more preferably a lower alkyl of from 1 to 7 carbons, and most preferably 1 to 4 carbons. Typical alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tertiary butyl, pentyl, hexyl and the like. The alkyl group may be substituted and some typical alkyl substituents include

15

hydroxyl, cyano, alkoxy, oxygen, sulfur, nitroxy, halogen, $-N(CH_3)_2$, amino, and -SH.

The term "methyl" refers to a saturated alkyl moiety of one carbon. The term "ethyl" refers to a saturated alkyl moiety of two carbons. The term "propyl" refers to a saturated alkyl moiety of three carbons. The term "butyl" refers to a saturated alkyl moiety of four carbons. The term "pentyl" refers to a saturated alkyl moiety of five carbons.

The term "aryl" refers to an aromatic group which has at least one ring having a conjugated pi electron system and includes both carbocyclic aryl (e.g. phenyl) and heterocyclic aryl groups (e.g. pyridine). Aryl moieties include monocyclic, bicyclic, and tricyclic rings, where each ring has preferably five or six members. The aryl moiety may be substituted and typical aryl substituents include halogen, trihalomethyl, hydroxyl, -SH, -OH, -NO₂, amine, thioether, cyano, alkoxy, alkyl, and amino.

The terms "heterocycle" or "heterocyclic" refer to compounds that form a ring and contain up to four hetero atoms, the remainder of the atoms forming the ring being carbon. Thus, for example, each ring in the structure can contain zero, one, two, three, or four nitrogen, oxygen, or sulfur atoms within the ring. The ring can preferably 25 be saturated with hydrogen atoms, more preferably harbor one or more unsaturations, and most preferably contain an aryl conjugated pi electron system. The rings are preferably eleven, twelve, thirteen, or fourteen membered rings, more preferably eight, nine, or ten membered rings, and 30 most preferably five or six membered rings. Examples of such rings are furyl, thienyl, pyrrol, imidazolyl, indolyl, pyridinyl, thiadiazolyl, thiazolyl, piperazinyl, dibenzfuranyl, dibenzthienyl. The heterocyclic rings of the invention may be optionally substituted with one or

more functional groups which are attached commonly to such rings, such as, e.g., hydroxyl, bromo, fluoro, chloro, iodo, mercapto or thio, cyano, cyanoamido, alkylthio, heterocycle, aryl, heteroaryl, carboxyl, oxo, alkoxycarbonyl, alkyl, alkenyl, nitro, amino, alkoxyl, amido, and the like. Structures of some preferred heterocyclic rings are the fused rings that have been shown above.

The term "aldehyde" refers to a chemical moiety with 10 formula $-(R)_n$ -CHO, where R is selected from the group consisting of alkyl or aryl and n is 0 or 1.

The term "ketone" refers to a chemical moiety with formula $-(R)_n$ -CO-R', where R and R' are selected from the group consisting of alkyl or aryl and n is 0 or 1.

The term "carboxylic acid" refers to a chemical moiety with formula $-(R)_n$ -COOH, where R is selected from the group consisting of alkyl or aryl and n is 0 or 1.

The term "ester" refers to a chemical moiety with formula -(R),-COOR', where R and R' are independently selected from the group consisting of alkyl or aryl and n is 0 or 1.

The term "sulfone" refers to a chemical moiety with formula $-SO_2-R$, where R is selected from the group consisting of alkyl or aryl.

The term "pharmaceutically acceptable salt" refers to a formulation of a compound that does not cause significant irritation to an organism and does not abrogate the biological activity and properties of the compound. Pharmaceutical salts can be obtained by reacting a compound of the invention with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like.

The term "prodrug" refers to an agent that is converted into the parent drug in vivo. Prodrugs may be easier to administer than the parent drug in some situations. For example, the prodrug may be bioavailable by oral administration but the parent is not, or the prodrug may improve solubility to allow for intravenous administration.

A preferred embodiment of the invention relates to compound of the following formula,

10

$$R_{\bullet}$$
 R_{\bullet}
 (V)

where (a) R_1 as is described above for the substituent at the 1' position of the indole ring;

(b) R_2 , R_3 , R_4 , R_5 , and R_6 are independently selected from the group consisting of,

18

- (i) hydrogen;
- (ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten
 membered monocyclic or bicyclic heterocyclic ring, where
 the ring is optionally substituted with one or more
 10 halogen or trihalomethyl substituents;
 - (iv) a ketone of formula -CO- R_{20} , where R_{20} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring
- (v) a carboxylic acid of formula -(R21)n-15 COOH or ester of formula $-(R_{22})-COO-R_{23}$, where R_{21} , R_{22} , and R_{23} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (vi) halogen;
- (vii) an alcohol of formula $(R24)\,m$ -OH or an ether of formula $-(R_{24})_{\,n}$ -O- R_{25} , where R_{24} and R_{25} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (viii) $-NR_{26}R_{27}$, where R_{26} and R_{27} are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (ix) $-NHCOR_{28}$, where R_{28} is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

- (x) $-SO_2NR_{29}R_{30}$, where R_{29} and R_{30} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (xi) any two of R_3 , R_4 , R_5 , or R_6 taken together form a bicyclic or tricyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;
- (c) R_7 , R_8 , R_9 , and R_{10} are independently selected from the group consisting of,
 - (i) hydrogen;
- (ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten
 membered monocyclic or bicyclic heterocyclic ring, where
 the ring is optionally substituted with one or more
 20 halogen or trihalomethyl substituents;
 - (iv) an aldehyde or ketone of formula -CO- R_{31} , where R_{31} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- 25 (v) a carboxylic acid of formula -(R32)n-COOH or ester of formula $-(R_{33})_m-COO-R_{34}$, where R_{32} , R_{33} , and R_{34} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;
- 30 (vi) halogen;
 - (vii) an alcohol of formula $(R_{35})_m$ -OH or an ether of formula $-(R_{35})$ n-O-R₃₆, where R₃₅ and R₃₆ are independently chosen from the group consisting of alkyl or a

five or six membered heterocyclic ring and m and n are independently 0 or 1;

(viii) $-NR_{37}R_{38}$, where R_{37} and R_{38} are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

- (ix) $-NHCOR_{39}$, where R_{39} is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- $(x) \qquad -\text{SO2NR}_{40}R_{41}, \quad \text{where} \quad R_{40} \quad \text{and} \quad R_{41} \quad \text{are}$ selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (xi) any two of R_1 , R_8 , R_9 , or R_{10} taken together form a bicyclic or tricyclic heterocyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and
 - (d) R_{11} is hydrogen or alkyl;

10

provided that at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , or R_{10} is alkyl or provided that at least four of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , or R_{10} are not hydrogen.

In preferred embodiments of the invention as shown in structure V above, R_1 is preferably a lower alkyl, branched or unbranched, more preferably an unbranched lower alkyl (e.g., ethyl, propyl, isopropyl, butyl, tertiary butyl, pentyl), and most preferably a methyl moiety.

In other preferred embodiments one or more of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , and R_{10} of structure V are a heterocyclic ring. The heterocycle is preferably selected from the group consisting of five, six, eight, nine, ten, eleven, twelve, thirteen, and fourteen membered aryl or non-aryl rings. The heterocycles can be furyl, thienyl, pyrrol, imidazolyl, indolyl, pyridinyl, thiadiazolyl,

thiazolyl, piperazinyl, dibenzfuranyl, dibenzthienyl, 2-aminothiazol-4-yl, 2-amino-5-chlorothiazol-4-yl, 2-amino-thiadiazol-4-yl, 2,3-dioxopiperazinyl, 4-alkylpiperazinyl, 2-iodo-3-dibenzfuranyl, and 3-hydroxy-4-dibenzthienyl. R₂ preferably is lower alkyl, more preferably methyl, or phenyl or biphenyl preferably mono-substituted with halogen. R₃, R₄, R₅ and mono-R₆ preferably are selected from the group consisting of hydrogen, unsubstituated lower alkyls, halogen, methoxy, carboncyclic and ether. R11 is preferably hydrogen.

In especially preferred embodiments of structure V, R_1 is methyl and R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , and R_{11} are hydrogen, or R_1 and R_7 are methyl and R_2 , R_3 , R_4 , R_6 , R_9 , R_{10} , and R_{11} are hydrogen. Other especially preferred compounds are set forth in the tables and examples set forth herein.

In another aspect, the invention features a method of synthesizing an indolinone compound, where the method comprises the steps of:

20 (a) reacting an aldehyde of formula VI with an oxindol of formula VII,

VΙ

$$R_{i}$$
 R_{i}
 R_{i}
 R_{i}
 R_{i}
 R_{i}

22

VII

$$R_{\bullet}$$
 R_{\bullet}
 R_{\bullet}
 R_{\bullet}
 R_{\bullet}
 R_{\bullet}
 R_{\bullet}

where R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , and R_{11} are described herein; and

(b) separating the indolinone compound from the 5 aldehyde and oxindol reactants.

The term "synthesizing" defines a method of combining multiple compounds together and/or chemically modifying the compound(s) in a controlled environment. A controlled environment preferably includes a glass vessel, a stirring rod or bar, a heating or cooling source, and specific organic solvents.

The term "reacting" refers to mixing two compounds together in a controlled environment. The compounds that are mixed together and reacted with one another are termed "reactants".

The term "separating" describes methods of segregating compounds from one or more other compounds. Compounds can be separated from one another by using techniques known in the art which include, but are not limited to, column chromatography techniques and solvent phase separation techniques.

In another aspect, the invention features optionally substituted 3-[(tetrahydroindole-2-yl)methylene]-2-indolinone and 3-[(cyclopentano-b-pyrrol-2-yl)methylene]-25 2-indolinone compounds.

The term "optionally substituted" refers, for example, to a benzene ring that either harbors a hydrogen at

a particular position or optionally harbors another substituent at that position. The term "optionally substituted" refers to other molecules in addition to benzene. A ring structure, for example can be N-substituted or C-substituted.

The term "N-substituted" refers to a compound that harbors chemical substituents attached to a nitrogen atom in a ring of the indolinone.

The term "C-substituted" refers to a compound that 10 harbors chemical substituents attached to a carbon atom in the indolinone.

The term "independently selected" refers to a molecule that harbors one substituent chosen from a group of substituents.

A preferred embodiment of the invention relates to an indolinone compound of the following formula,

$$\begin{array}{c}
R_{3} \\
R_{4} \\
R_{5} \\
R_{7} \\
R_{10} \\
R_{10} \\
R_{10} \\
R_{2} \\
R_{3} \\
R_{4} \\
R_{5} \\
R_{5} \\
R_{7} \\
R_{7} \\
R_{10} $

24

IX

$$R_{3}$$
 R_{3}
 R_{4}
 R_{5}
 R_{4}
 R_{5}
 R_{5}
 R_{4}
 R_{5}
 where (a) R_1 is selected from the group consisting of,

- (i) hydrogen;
- (ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten 10 membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (iv) ketone of formula $-CO-R_{11}$, where R_{11} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (v) a carboxylic acid of formula $-(R_{12})_n$ -COOH or ester of formula $-(R_{13})_m$ -COO- R_{14} , where R_{12} , R_{13} , and R_{14} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;
 - (vi) a sulfone of formula -(SO2)- R_{15} , where R_{15} is selected from the group consisting of alkyl or a

WO 98/07695

five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;

- $(\text{vii}) \qquad -(R_{16})_n (\text{indole-1-yl}) \quad \text{or} \quad -(R_{17})_m \text{CHOH-} \\ (R_{18})_p (\text{indole-1-yl}), \quad \text{where the indole moiety is optionally} \\ 5 \quad \text{substituted with an aldehyde and} \quad R_{16}, \quad R_{17}, \quad \text{and} \quad R_{18} \quad \text{are alkyl} \\ \text{and} \quad n, \quad m, \quad \text{and} \quad p \quad \text{are independently} \quad 0 \quad \text{or} \quad 1;$
- (viii) taken together with a 2' substituent
 of the indole ring form a tricyclic moiety, where each
 ring in the tricyclic moiety is a five or six membered
 10 heterocyclic ring;
 - (b) R_2 , R_3 , R_3 , R_4 , R_4 , R_5 , R_5 , R_6 , and R_6 are independently selected from the group consisting of,
 - (i) hydrogen;
- (ii) alkyl that is optionally substituted

 15. with a monocyclic or bicyclic five, six, eight, nine, or
 ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or
 trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten 20 membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- (iv) ketone of formula $-CO-R_{20}$, where R_{20} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
 - (v) a carboxylic acid of formula $-(R_{21})_n$ -COOH or ester of formula $-(R_{22})$ -COO- R_{23} , where R_{21} , R_{22} , and R_{23} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (vi) halogen;
 - (vii) an alcohol of formula $(R_{24})_m$ -OH or an ether of formula $-(R_{24})_n$ -O- R_{25} , where R_{24} and R_{25} are independently selected from the group consisting of alkyl and a five or

six membered heterocyclic ring and m and n are independently 0 or 1;

- $(\text{viii}) \quad -\text{NR}_{26}\text{R}_{27}, \text{ where } \text{R}_{26} \text{ and } \text{R}_{27} \text{ are independently selected from the group consisting of hydrogen,} \\ 5 \quad \text{oxygen, alkyl, and a five or six membered heterocyclic ring;} \\$
- (ix) $-NHCOR_{2\theta}$, where $R_{2\theta}$ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - $(x) \quad \text{-SO2NR}_{29}R_{30}, \text{ where } R_{29} \text{ and } R_{30} \text{ are selected}$ from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (xi) any two of R₃, R₃, R₄, R₄, R₅, R₅, R₆, or R₆.
 15 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;
- (c) $R_{7},\ R_{8},\ R_{9},\ \mbox{and}\ \ R_{10}$ are independently selected 20 from the group consisting of,
 - (i) hydrogen;
- (ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten
 membered monocyclic or bicyclic heterocyclic ring, where
 the ring is optionally substituted with one or more
 30 halogen or trihalomethyl substituents;
 - (iv) ketone of formula $-CO-R_{31}$, where R_{31} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

- (v) a carboxylic acid of formula $-(R_{32})_n$ -COOH or ester of formula $-(R_{33})_m$ -COO- R_{34} , where R_{32} , R_{33} , and R_{34} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;
 - (vi) halogen;
- (vii) an alcohol of formula $(R_{35})_m$ -OH or an ether of formula $-(R_{35})_n$ -O- R_{36} , where R_{35} and R_{36} are independently chosen from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (viii) $-NR_{37}R_{38}$, where R_{37} and R_{38} are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
 - (ix) -NHCOR₃₉, where R_{39} is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- 20 (x) $-SO2NR_{40}R_{41}$, where R_{40} and R_{41} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (xi) any two of R₇, R₈, R₉, or R₁₀ taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and
 - (d) R_{11} is hydrogen or alkyl.
- Another preferred embodiment of the invention relates to indolinone compounds of structures VIII and IX, where R_1 , R_2 , R_3 , R_3 , R_4 , R_4 , R_5 , R_5 , R_6 , R_6 , R_6 , R_7 , R_8 , R_9 , R_{10} , and R_{11} are hydrogen.

In another preferred embodiment, the invention relates to oxidolinone compounds of structures VIII and

IX, where R_8 is bromine, chlorine, or NH2 and R_1 , R_2 , R_3 , R_3 , R_4 , R_4 , R_5 , R_5 , R_6 , R_6 , R_6 , R_7 , R_9 , R_{10} , and R_{11} are hydrogen.

In yet another preferred embodiment, the invention relates to indolinone compounds of structures VIII and IX, where R_1 is methyl and R_1 , R_2 , R_3 , R_3 , R_4 , R_4 , R_5 , R_5 , R_6 , R_6 , R_7 , R_9 , R_{10} , and R_{11} are hydrogen.

In another aspect, the invention features a method of synthesizing an indolinone compound, where the method 10 comprises the steps of:

(a) reacting an aldehyde of formula \boldsymbol{X} or \boldsymbol{XI} with an oxindol of formula \boldsymbol{XII} ,

Х

15 XI

$$R_{i}$$
 R_{i}
 R_{i}
 R_{i}
 R_{i}

XII

WO 98/07695

where R_1 , R_2 , R_3 , R_3 , R_4 , R_4 , R_5 , R_5 , R_6 , R_6 , R_6 , R_7 , R_8 , R_9 , R_{10} , and R_{11} are described herein; and

- (b) separating the indolinone compound from the aldehyde and oxindole reactants.
- In another aspect, the invention features an indolinone compound having a substituent at the 5 position of the oxindole ring, where the substituent at the 5 position of the oxindole ring is selected from the group consisting of:
- (a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- (c) a ketone of formula $-CO-R_{10}$, where R_{10} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (d) a carboxylic acid of formula $-(R_{11})\,n$ -COOH or ester of formula $-(R_{12})\,-$ COO- R_{13} , where R_{11} , R_{12} , and R_{13} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (e) halogen;
- (f) an alcohol of formula $(R_{14})_m$ -OH or an ether of formula $-(R_{14})_m$ -O- R_{15} , where R_{14} and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

30

(g) $-NR_{16}R_{19}$, where R_{16} and R_{19} are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

- (h) -NHCOR₁₈, where R₁₈ is selected from the 5 group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- (i) $-SO_2NR_{19}R_{20}$, where R_{19} and R_{20} are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (j) any two of R_4 , R_5 , R_6 , or R_7 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring.

A preferred embodiment of the invention relates to a compound of the following formula,

$$\begin{array}{c|c}
R_{3} & R_{2} & R_{1} \\
R_{4} & R_{2} & R_{1}
\end{array}$$

$$\begin{array}{c|c}
R_{4} & R_{2} & R_{3} \\
R_{4} & R_{1} & R_{2}
\end{array}$$

(XIII)

20

where (a) R_5 is selected from the group consisting of,

(i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is option ally substituted with one or more halogen, or trihalomethyl substituents;

- (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- 5 (iii) a ketone of formula $-CO-R_{10}$, where R_{10} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (iv) a carboxylic acid of formula $-(R_{11}) n COOH$ or ester of formula $-(R_{12}) COO R_{13}$, where R_{11} , R_{12} , and 10 R_{13} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (v) halogen;
- (vi) an alcohol of formula $(R_{14})_m$ -OH or an ether of formula $-(R_{14})_n$ -O- R_{15} , where R_{14} and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (vii) $-NR_{16}R_{17}$, where R_{16} and R_{17} are independ-20 ently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (viii) $-NHCOR_{10}$, where R_{10} is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (ix) $-SO_2NR_{19}R_{20}$, where R_{19} and R_{20} are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (x) any two of R_4 , R_5 , R_6 , or R_7 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the oxindole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;

- (b) R_1 is selected from the group consisting of a five, six, eight, nine, and ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more substituents selected from the group consisting of
- (i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
 - (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- 15 (iii) a ketone of formula $-CO-R_{21}$, where R_{21} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (iv) a carboxylic acid of formula $-(R_{22})_n$ -COOH or ester of formula $-(R_{23})$ -COO- R_{24} , where R_{22} , R_{23} , and R_{24} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (v) halogen;
- (vi) an alcohol of formula (R_{25}) m-OH or an ether of formula $-(R_{25})$ n-O-R₂₆, where R₂₅ and R₂₆ are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (vii) $-NR_{27}R_{28}$, where R_{27} and R_{28} are independ-30 ently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
 - $\mbox{(viii)} \qquad -\mbox{NHCOR}_{29}, \mbox{ where } \mbox{R}_{29} \mbox{ is selected from the} \\ \mbox{group consisting of alkyl, and a five or six membered}$

heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;

- $(ix) \qquad -SO_2NR_{30}R_{31}, \quad \text{where} \quad R_{30} \quad \text{and} \quad R_{31} \quad \text{are}$ selected from the group consisting of hydrogen, alkyl, and 5 a five or six membered heterocyclic ring;
 - (c) $R_4,\ R_6,\ and\ R_7$ are independently selected from the group consisting of,
- (i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six,
 10 eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten
 membered monocyclic or bicyclic heterocyclic ring, where
 15 the ring is optionally substituted with one or more
 halogen or trihalomethyl substituents;
 - (iii) a ketone of formula -CO- R_{32} , where R_{32} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- 20 (iv) a carboxylic acid of formula $-(R_{33})\,n-$ COOH or ester of formula $-(R_{34})\,-$ COO- R_{35} , where R_{33} , R_{34} , and R_{35} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- 25 (v) halogen;

30

- (vi) an alcohol of formula $(R_{36})\,m$ -OH or an ether of formula $-(R_{36})\,_n$ -O- R_{37} , where R_{36} and R_{37} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (vii) $-NR_{38}R_{39}$, where R_{38} and R_{39} are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;

- (viii) $-NHCOR_{40}$, where R_{40} is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- 5 (ix) $-SO_2NR_{41}R_{42}$, where R_{41} and R_{42} are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring; and
 - (d) R₂ is hydrogen or alkyl.

In preferred embodiments of the invention shown in structure XIII above one or more of R_1 , R_4 , R_5 , R_6 , or R_7 are a heterocyclic ring. Preferred heterocycles of the invention are described herein.

Another preferred embodiment of the invention shown in structure XIII above is an indolinone compound, where 15 R_1 is (3,5-dimethylpyrrol)-2-yl, R_5 is -COOH, and R_2 , R_4 , R_6 , and R_7 are hydrogen.

Another preferred embodiment of the invention shown in structure XIII above is an indolinone compound, where R_1 is (3,5-diethylpyrrol)-2-yl, R_5 is -COOH, and R_2 , R_4 , R_6 , and R_7 are hydrogen.

Another preferred embodiment of the invention shown in structure XIII above is an indolinone compound, where R_1 is (3,5-diisopropylpyrrol)-2-yl, R_5 is -COOH, and R_2 , R_4 , R_6 , and R_7 are hydrogen.

Another preferred embodiment of the invention shown in structure XIII above is an indolinone compound, where R_1 is (3,5-dimethylpyrrol)-2-yl, R_5 is $-(CH_2)_2COOH$, and R_2 , R_4 , R_6 , and R_7 are hydrogen.

Another preferred embodiment of the invention shown in structure XIII above is an indolinone compound, where R_1 is (5-methylthiophene)-2-yl, R_5 is -COOH, and R_2 , R_4 , R_6 , and R_7 are hydrogen.

In another aspect, the invention features a method of synthesizing an indolinone compound, where the method comprises the steps of:

(a) reacting an aldehyde of formula XIV with an oxindole of formula XV,

XIV

ΧV

$$\begin{array}{c|c}
R_{3} & R_{4} \\
R_{4} & R_{7}
\end{array}$$

where R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , and R_{11} are as 10 described herein; and

(b) separating the indolinone compound from the aldehyde and oxindole reactants.

In another aspect, the invention features an indolinone compound having a substituent at the 3 position of the oxindole ring, where the substituent at the 3 position of the oxindole ring is selected from the group consisting of five-membered or six-membered heterocyclic rings. The oxindolonine is further substituted with groups enhancing hydrosolubility as set forth below.

A preferred embodiment of the invention relates to a compound of the following formula:

 $(OR_1)_m$ R_3 P R_3 R_4 R_4 R_5 R_4 R_5 R_5 R_7 R_8

wherein

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- (a) A is a five membered heterocyclic ring selected from the following group consisting of thiophene, pyrrole,
 5 pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, and tetrazole
 - (b) m is zero, 1, or 2;
 - (c) R_1 is hydrogen, C_1 - C_6 alkyl or C_2 - C_6 alkanoyl;
- (d) one of R_2 and R_3 independently is hydrogen and the other is a substituent selected from:
 - (1) a C_1 - C_6 alkyl group substituted by 1, 2 or 3 hydroxy groups;
 - (2) SO_3R_4 in which R_4 is hydrogen or C_1 - C_6 alkyl unsubstituted or substituted by 1, 2 or 3 hydroxy groups;
 - (3) SO_2NHR_5 in which R_5 is as R_4 defined above or $A_5 = (CH_2)_n N(C_1 C_6 = A + C_6)_n$ group in which n is 2 or 3;
 - (4) $COOR_6$ in which R_6 is C_1-C_6 alkyl unsubstituted or substituted by phenyl or by 1, 2 or 3 hydroxy groups or phenyl;

WO 98/07695

- (5) CONHR, in which R, is hydrogen, phenyl or C_1 C_6 alkyl substituted by 1, 2 or 3 hydroxy groups or by phenyl;
- (6) NHSO₂R₈ in which R₈ is C_1 - C_6 alkyl or phenyl unsubstituted or substituted by halogen or by C_1 - C_4 alkyl;
 - (7) $N(R_9)_2$, NHR, or OR, wherein R_9 is C_2 - C_6 alkyl substituted by 1, 2 or 3 hydroxy groups;
 - (8) NHCOR₁₀, OOCR₁₀ or CH_2OOCR_{10} in which R_{10} is C_1 - C_6 alkyl substituted by 1, 2 or 3 hydroxy groups;
- 10 (9) NHCONH₂; NH-C(NH₂)=NH; $C(NH_2)=NH$; $C(NH_2)=NH$; $CH_2NHC(NH_2)=NH$; CH_2NH_2 ; OPO(OH)₂; $CH_2OPO(OH)_2$; PO(OH)₂; or a



group wherein X is selected from the group consisting of CH_2 , SO_2 , CO, or $NHCO(CH_2)_p$ in which p is 1,2, or 3 and Z is 15 CH2, O or $N-R_{11}$ in which R_{11} is hydrogen or is as R_9 defined above.

The term "alkanoyl" refers to a chemical moiety with formula $-(R)_n$ -CO-R', where R and R' are selected from the group consisting of alkyl or aryl and n is 0 or 1.

Inhibitors of protein kinase catalytic activity are known in the art. Small molecule inhibitors typically block the binding of substrates by tightly interacting with the protein kinase active-site. Indolinone compounds, for example, can bind to the active-site of a protein kinase and inhibit the molecule effectively, as measured by inhibition constants on the order of 10⁻⁶ M.

A preferred embodiment of the invention relates to an hydrosoluble indolinone compound that inhibits the catalytic activity of a FLK protein kinase. The indolinone preferably inhibits the catalytic activity of the FLK protein kinase with an IC_{50} less than 50 μ M, more prefera-

bly with an IC $_{50}$ less than 5 $\mu M,$ and most preferably with an IC $_{50}$ less than 0.5 $\mu M.$

In another aspect, the invention features a method of synthesizing a hydrosoluble indolinone compound, where the method comprises the steps of:

(a) reacting an aldehyde of formula XVI with an oxindole of formula XVII,

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XVII

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where

- (a) A is a five or six membered ring comprised of atoms selected from the group consisting of oxygen,20 carbon, sulfer and nitrogen
 - (b) m is zero, 1, or 2;

- (c) R_1 is hydrogen, C_1 - C_6 alkyl or C_2 - C_6 alkanoyl;
- (d) one of R_2 and R_3 independently is hydrogen and the other is a substituent selected from:
- (1) a $C_1 C_6$ alkyl group substituted by 1, 2 or 3 5 hydroxy groups;
 - (2) SO_3R_4 in which R_4 is hydrogen or C_1 - C_6 alkyl unsubstituted or substituted by 1, 2 or 3 hydroxy groups;
 - (3) SO_2NHR_5 in which R_5 is as R_4 defined above or $a (CH_2)_n N(C_1 C_6 \text{ alkyl})_2$ group in which n is 2 or 3;
- 10 (4) COOR $_6$ in which R $_6$ is C $_1$ -C $_6$ alkyl unsubstituted or substituted by phenyl or by 1, 2 or 3 hydroxy groups or phenyl;
- (5) CONHR, in which R, is hydrogen, phenyl or C_1 C_6 alkyl substituted by 1, 2 or 3 hydroxy groups or by phenyl;
 - (6) NHSO₂R₈ in which R₈ is C_1-C_6 alkyl or phenyl unsubstituted or substituted by halogen or by C_1-C_4 alkyl;
 - (7) $N(R_9)_2$, NHR, or OR, wherein R, is C_2 - C_6 alkyl substituted by 1, 2 or 3 hydroxy groups;
- 20 (8) NHCOR₁₀, OOCR₁₀ or CH_2OOCR_{10} in which R_{10} is C_1 C_6 alkyl substituted by 1, 2 or 3 hydroxy groups;
 - (9) $NHCONH_2$; $NH-C(NH_2)=NH$; C(NH)=NH; $CH_2NHC(NH_2)=NH$; CH_2NH_2 ; $OPO(OH)_2$; $CH_2OPO(OH)_2$; $PO(OH)_2$; or a



- group wherein X is selected from the group consisting of CH_2 , SO_2 , CO, or $NHCO(CH_2)_p$ in which p is 1,2, or 3 and Z is CH2, O or $N-R_{11}$ in which R_{11} is hydrogen or is as R_9 defined above; and
- (b) separating the indolinone compound from the 30 aldehyde and oxindole reactants.

Another aspect of the invention features a pharmaceutical composition comprising an oxidolinone compound of

the invention and a physiologically acceptable carrier or diluent.

In the embodiments set forth below, several preferred subclasses of compounds having activity against Flk are set forth. Thus, in one embodiment, the invention provides compounds having the formula:

wherein

10 R_1 is hydrogen or alkyl (preferably lower alkyl, more preferably methyl);

R2 is oxygen or sulfur;

R₃ is hydrogen or methyl;

 R_4 , R_5 , R_6 , and R_7 are each independently selected from the group consisting of hydrogen (preferably at least two or three of R_4 , R_5 , R_6 and R_7 are hydrogen), alkyl (preferably lower alkyl, more preferably methyl), halogen, NO_2 , and NRR';

 R_2 , R_3 , R_4 , R_5 , and R_6 are each independently selected from the group consisting of hydrogen, alkyl, halogen, NO_2 , NRR' (where taken together NRR^1 may form a five or six member non-aromatic heterocyc optionally substituted with COH), OH, $ORNRR^1$, and OR;

R is hydrogen, alkyl or aryl; and

R' is hydrogen, alkyl or aryl.

In another embodiment, the invention provides compounds having the formula:

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wherein

 $\ensuremath{R_{1}}$ is hydrogen or alkyl (preferably lower alkyl, more preferably methyl);

10 R_2 is oxygen or sulfer;

R₃ is hydrogen or methyl;

 R_4 , R_5 , R_6 , and R_7 are each independently selected from the group consisting of hydrogen, alkyl (preferably lower alkyl, more preferably methyl), halogen, and NRR';

 R_{2} , R_{3} , R_{4} , and R_{5} , are each independently selected from the group consisting of hydrogen, alkyl, halogen, and $(alkyl)_nCO_2R$;

R is hydrogen, alkyl or aryl; and

R' is hydrogen, alkyl or aryl.

In another embodiment, the invention provides compounds having the formula:

42

$$R_{5}$$
 R_{6}
 R_{7}
 R_{7}
 R_{1}
 R_{1}

wherein

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 R_1 , R_2 , and R_3 , are each independently selected from the group consisting of hydrogen, alkyl, halogen, and 5 (alkyl) $_nCO_2R$;

 R_4 , R_5 , R_6 , and R_7 are each independently selected from the group consisting of hydrogen, alkyl (preferably lower alkyl, more preferably methyl), halogen, and NRR';

R₈ and R₉ are independently hydrogen or alkyl;

R is hydrogen, alkyl or aryl; and

R' is hydrogen, alkyl or aryl.

In another embodiment, the invention provides compounds having the formula:

(XVIII)

wherein

 R_1 ., R_2 ., R_3 ., R_4 . and R_7 are each independently selected from the group consisting of hydrogen, alkyl (preferably lower alkyl, more preferably methyl), halogen and NRR';

43

 R_{θ} and R_{θ} are independently hydrogen or alkyl; R is hydrogen, alkyl or aryl; and R' is hydrogen, alkyl or aryl.

In another aspect, the invention features a method of synthesizing an indolinone compound, where the method comprises the steps of:

- (a) reacting an appropriate aldehyde with an appropriate oxindole,
- (b) separating the indolinone compound from the 10 aldehyde and oxindole reactants.

In another aspect, the invention features an indolinone compound, salt, ester, amide, prodrug, isomer, or metabolite thereof that modulates the catalytic activity of a protein kinase.

The term "modulates" refers to the ability of a compound to alters the catalytic activity of a protein kinase. A modulator preferably activates the catalytic activity of a protein kinase, more preferably activates or inhibits the catalytic activity of a protein kinase depending on the concentration of the compound exposed to the protein kinase, or most preferably inhibits the catalytic activity of a protein kinase.

The term "protein kinase" defines a class of proteins that regulate a variety of cellular functions. Protein kinases regulate cellular functions by reversibly phosphorylating protein substrates which thereby changes the conformation of the substrate protein. The conformational change modulates catalytic activity of the substrate or its ability to interact with other binding partners.

The term "catalytic activity", in the context of the invention, defines the rate at which a protein kinase phosphorylates a substrate. Catalytic activity can be measured, for example, by determining the amount of a substrate converted to a product as a function of time.

Phosphorylation of a substrate occurs at the active-site of a protein kinase. The active-site is normally a cavity in which the substrate binds to the protein kinase and is phosphorylated.

A preferred embodiment of the invention relates to an indolinone compound that inhibits the catalytic activity of a FLK protein kinase. The indolinone preferably inhibits the catalytic activity of the FLK protein kinase with an IC50 less than 50 μM , more preferably with an IC50 10 less than 5 μM , and most preferably with an IC50 less than 0.5 µM.

The term "FLK" refers to a protein kinase that phosphorylates protein substrates on tyrosine residues. The FLK protein kinase regulates cellular functions in 15 response to the VEGF growth factor. These cellular functions include, but are not limited to, cellular proliferation, and in particular, blood vessel proliferation in tissues.

The term "IC₅₀", in the context of the invention, 20 refers to a parameter that describes the concentration of a particular indolinone required to inhibit 50% of the FLK protein kinase catalytic activity. The IC₅₀ parameter can be measured using an assay described herein and by varying the concentration of a particular indolinone compound.

Another aspect of the invention features a pharmaceutical composition comprising, consisting essentially of, or consisting of an indolinone compound, salt, ester, amide, prodrug, isomer, or metabolite thereof invention and a physiologically acceptable carrier or 30 diluent.

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The term "pharmaceutical composition" refers to a mixture of an indolinone compound of the invention with other chemical components, such as diluents or carriers. The pharmaceutical composition facilitates administration

of the compound to an organism. Multiple techniques of administering a compound exist in the art including, but not limited to, oral, injection, aerosol, parenteral, and topical administration. Pharmaceutical compositions can also be obtained by reacting compounds with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like.

The term "physiologically acceptable" defines a carrier or diluent that does not cause significant irritation to an organism and does not abrogate the biological activity and properties of the compound.

The term "carrier" defines a chemical compound that facilitates the incorporation of a compound into cells or tissues. For example dimethyl sulfoxide (DMSO) is a commonly utilized carrier as it facilitates the uptake of many organic compounds into the cells or tissues of an organism.

The term "diluent" defines chemical compounds diluted in water that will dissolve the compound of interest as well as stabilize the biologically active form of the compound. Salts dissolved in buffered solutions are utilized as diluents in the art. One commonly used buffered solution is phosphate buffered saline because it mimics the salt conditions of human blood. Since buffer salts can control the pH of a solution at low concentrations, a buffered diluent rarely modifies the biological activity of a compound.

Another aspect of the invention features a method of preventing or treating an abnormal condition in an organism. The abnormal condition is associated with an aberration in a signal transduction pathway characterized by an interaction between a protein kinase and a natural binding

46

partner. The method comprises the following steps: (a) administering a compound of the invention to an organism; and (b) promoting or disrupting the abnormal interaction.

The term "preventing" refers to a method of barring the organism from acquiring the abnormal condition.

The term "treating" refers to a method of alleviating or abrogating the abnormal condition in the organism.

The term "organism" relates to any living entity comprised of at least one cell. An organism can be as simple as one eukaryotic cell or as complex as a mammal.

The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation, or cell survival.

Aberrant cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

Aberrant differentiation conditions include, but are not limited to neurodegenerative disorders, slow wound healing rates, and tissue grafting techniques.

Aberrant cell survival conditions relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the protein kinases could lead to cell immortality or premature cell death.

Cell proliferation, differentiation, and survival are phenomena simply measured by methods in the art. These methods can involve observing the number of cells or the appearance of cells under a microscope with respect to time (days).

47

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques, and carrier techniques.

The aberrant condition can also be prevented or treated by administering a group of cells having an aberration in a signal transduction process to an organism. The effect of administering a compound on organism function can then be monitored. The art contains multiple methods of introducing a group of cells to an organism as well as methods of administering a compound to an organism. The organism is preferably a frog, more preferably a mouse, rat, rabbit, guinea pig, or goat, and most preferably a monkey or ape.

The term "signal transduction pathway" refers to the molecules that propagate an extracellular signal through the cell membrane to become an intracellular signal. This signal can then stimulate a cellular response. The polypeptide molecules involved in signal transduction processes are typically receptor and non-receptor protein kinases, receptor and non-receptor protein phosphatases, nucleotide exchange factors, and transcription factors.

48

The term "aberration", in conjunction with a signal transduction process, refers to a protein kinase that is over- or under-expressed in an organism, mutated such that its catalytic activity is lower or higher than wild-type protein kinase activity, mutated such that it can no longer interact with a natural binding partner, is no longer modified by another protein kinase or protein phosphatase, or no longer interacts with a natural binding partner.

The term "natural binding partner" refers to a 10 polypeptide that normally binds to the intracellular region of a protein kinase in a cell. These natural binding partners can play a role in propagating a signal in a protein kinase signal transduction process. 15 natural binding partner can bind to a protein kinase intracellular region with high affinity. High affinity represents an equilibrium binding constant on the order of 10-6 M or less. However, a natural binding partner can also transiently interact with a protein kinase intracel-20 lular region and chemically modify it. Protein kinase natural binding partners are chosen from a group consisting of, but not limited to, src homology 2 (SH2) or 3 (SH3) domains, other phosphoryl tyrosine binding (PTB) domains, and other protein kinases or25 phosphatases.

The term "promoting or disrupting the abnormal interaction" refers to a method that can be accomplished by administering a compound of the invention to cells or tissues in an organism. A compound can promote an interaction between a protein kinase and natural binding partners by forming favorable interactions with multiple amino acids at the complex interface. Alternatively, a compound can inhibit an interaction between a protein kinase and natural binding partners by compromising

PCT/US97/14736

favorable interactions formed between amino acids at the complex interface.

A preferred embodiment of the invention relates to the method of treating an abnormal condition in an organism, where the organism is a mammal.

The term "mammal" refers preferably to such organisms as mice, rats, rabbits, guinea pigs, and goats, more preferably to monkeys and apes, and most preferably to humans.

Another preferred embodiment of the invention relates to a method of treating or preventing an abnormal condition associated with the *FLK* protein kinase.

Another preferred embodiment of the invention relates to an indolinone compound that inhibits the catalytic activity of a platelet derived growth factor protein kinase. The indolinone preferably inhibits the catalytic activity of the platelet derived growth factor protein kinase with an IC_{50} less than 50 μ M, more preferably with an IC_{50} less than 5 μ M, and most preferably with an IC_{50} less than 0.5 μ M.

The term "platelet derived growth factor" refers to a protein kinase that phosphorylates substrates on tyrosine residues. The platelet derived growth factor protein kinase regulates cellular functions in response to the PDGF growth factor. These cellular functions include, but are not limited to, cellular proliferation.

The chemical formulae referred herein may exhibit the phenomena of tautomerism or structural isomerism. For example, the compounds described herein may be adopt a cis or trans conformation about the double bond connecting the indolinone 3-substituent to the indolinone ring, or may be mixtures of cis and trans isomers. As the formulae drawing within this specification can only represent one possible tautomeric or structural isomeric form, it should

50

be understood that the invention encompasses any tautomeric or structural isomeric form, or mixtures thereof,
which possesses the ability to regulate, inhibit and/or
modulate tyrosine kinase signal transduction or cell
proliferation and is not limited to any one tautomeric or
structural isomeric form utilized within the formulae
drawing.

In addition to the above-described compounds, the invention is further directed, where applicable, to solvated as well as unsolvated forms of the compounds (e.g. hydrated forms) having the ability to regulate and/or modulate cell proliferation.

The compounds described herein may be prepared by any process known to be applicable to the preparation of chemically-related compounds. Suitable processes are illustrated in the examples. Necessary starting materials may be obtained by standard procedures of organic chemistry.

An individual compound's relevant activity and efficacy as an agent to affect receptor tyrosine kinase mediated signal transduction may be determined using available techniques. Preferentially, a compound is subjected to a series of screens to determine the compound's ability to modulate, regulate and/or inhibit cell proliferation. These screens, in the order in which they are conducted, include biochemical assays, cell growth assays and in vivo experiments.

The summary of the invention described above is not limiting and other features and advantages of the invention will be apparent from the following detailed description of the invention, and from the claims.

Brief Description of the Drawings and Tables

Figure 1 shows illustrative type A oxindoles.

Figure 2 shows illustrative type B aldehydes.

Table 1 depicts examples of compounds of the invention. The table illustrates the molecular structure of each indolinone, the molecular weight of the compound, and the chemical formula of the compound.

Table 2 depicts the biological activity of select compounds of the invention. Listed are the chemical structure of the compound with IC_{50} values measured in *FLK*-1 biological inhibition assays.

Table 3 shows preferred indole based aldehydes that can be used in the present invention.

Table 4 shows preferred oxindoles that can be used in the present invention.

Table 5 depicts examples of compounds of the invention. The table illustrates the molecular structure of
each indolinone, the molecular weight of the compound, and
the chemical formula of the compound.

Tables 6 and 7 depicts the biological activity of select compounds of the invention. Listed are the chemi- cal structure of the compound with IC_{50} values measured in FLK-1 and platelet derived growth factor protein kinase (PDGFR) biological inhibition assays.

Table 8 depicts examples of compounds of the invention. The table illustrates the molecular structure of exemplary indolinones and the biological activity of select compounds of the invention. Listed are the chemical structure of the compound with IC₅₀ values measured in FLK-1 biological inhibition assays.

Table 9 lists exemplary compounds of the invention.

Table 10 shows FLK activity data for illustrative compounds of the invention.

Table 11 shows type A oxindols.

Table 12 shows type B aldehydes.

52

Table 13 shows the names of several indolinone compounds of the present invention.

Table 14 shows kinase data for the compounds listed in Table 13 as determined using the assays described 5 herein.

Detailed Description of the Invention

The invention is directed in part towards designing protein kinase inhibitors that obliterate tumors by severing their sources of sustenance. The inhibitors are designed to specifically bind protein kinases over-expressed in the vasculature that supply tumors with sustenance. One such protein kinase target is FLK-1, which is over-expressed in the proliferating endothelial cells of a growing tumor, but not in the surrounding quiescent endothelial cells. Plate et al., 1992, Nature 359:845-848.

regulator for endothelial cell proliferation as well as normal and pathological angiogenesis. Klagsburn and Soker, 1993, Current Biology 3:699-702. Thus, compounds that specifically inhibit the FLK protein kinase are potential anti-cancer agents as they may decrease the vasculature that nourishes tumors. These inhibitors will most likely result in minimizing and even obliterating solid tumors. In addition, compounds that specifically inhibit FLK will potentially represent a new generation of cancer therapeutics as they will most likely cause few side effects. These potential properties are a welcome improvement over the currently utilized cancer therapeutics that cause multiple side effects and deleteriously weaken patients.

53

Synthesis of Indolinone Compounds

The indolinone compounds of the invention are synthesized by reacting an aldehyde with an oxindol as shown in the examples provided herein. Descriptions of methods for synthesizing indolinone compounds are provided in the examples described herein. The examples fully describe the solvents, temperatures, separation techniques, and other conditions utilized for the invention. Other synthetic techniques, such as those described in International patent publications WO 96/22976, published August 1, 1996 by Ballinari et al., and WO 96/40116, published December 19, 1996 by Tang et al. may also be used or adapted by those skilled in the art to make the compounds of the present invention. Descriptions of the methods used to specifically synthesize the indolinone compounds of the invention, are disclosed herein.

Biological Activity of Indolinone Compounds

Indolinone compounds of the invention can be tested for their ability to activate or inhibit protein kinases in biological assays. The methods used to measure indolinone modulation of protein kinase function are described herein. Indolinone compounds of the invention were tested for their ability to inhibit the FLK protein kinase. The biological assay and results of these inhibition studies are reported herein.

Target Diseases to be Treated by Indolinone Compounds

Protein kinases are essential regulatory molecules that control a variety of cellular functions. For this reason, any alteration in the function of a protein kinase can cause an abnormal condition in an organism. One of the many functions controlled by protein kinases is cell proliferation.

54

Alterations in the function of a protein kinase that normally regulates cell proliferation can lead to enhanced or decreased cell proliferative conditions evident in certain diseases. Aberrant cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, restenosis, diabetes mellitus, and inflammation.

Fibrotic disorders and mesangial cell proliferative disorders are described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

Angiogenic and vasculogenic disorders result from excess proliferation of blood vessels. Blood vessel 15 proliferation is necessary in a variety of normal physiclogical processes such as embryonic development, corpus luteum formation, wound healing and organ regeneration. However, blood vessel proliferation is also essential in cancer tumor development. Other examples of blood vessel 20 proliferative disorders include arthritis, where new capillary blood vessels invade the joint and destroy cartilage. In addition, blood vessel proliferative diseases include ocular diseases, such as diabetic retinopathy, where new capillaries in the retina invade the 25 vitreous, bleed and cause blindness. Conversely, disorders related to the shrinkage, contraction or closing of blood vessels, such as restenosis, are also implicated in adverse regulation of RPKs or RPPs.

Moreover, vasculogenesis and angiogenesis are associ30 ated with the growth of malignant solid tumors and metastasis. A vigorously growing cancer tumor requires a
nutrient and oxygen rich blood supply to continue growing.
As a consequence, an abnormally large number of capillary
blood vessels often grow in concert with the tumor and act

55

as supply lines to the tumor. In addition to supplying nutrients to the tumor, the new blood vessels embedded in a tumor provide a gateway for tumor cells to enter the circulation and metastasize to distant sites in the organism. Folkman, 1990, J. Natl. Cancer Inst. 82:4-6.

Angiogenic and vasculogenic disorders are closely linked to the FLK protein kinase. FLK-1 is activated upon binding VEGF, a strong regulator for endothelial cell proliferation as well as normal and pathological angiogen-Klagsburn and Soker, 1993, Current Biology 3:699-702. Thus, compounds that specifically inhibit the FLK protein kinase are potential anti-cancer agents as they may decrease the vasculature that nourishes tumors. These inhibitors will most likely result in minimizing and even obliterating solid tumors. In addition, compounds that specifically inhibit FLK will potentially represent a new generation of cancer therapeutics as they will most likely cause few side effects. These potential properties are a significant improvement over the currently utilized 20 cancer therapeutics that cause multiple side effects and deleteriously weaken patients.

In addition to cell proliferation, some RPKs and RPPs regulate the penultimate cellular functions, cell survival and cell death. Glial derived growth factor (GDNF) activates c-ret, for example, by bringing multiple c-ret receptors together into close proximity and promoting cross phosphorylation of the intracellular regions. Signal transduction molecules that form a complex with c-ret as a result of these phosphoryl moieties, such as grb-30 2, sos, ras, and raf, propagate a signal in the cell that promotes neural survival. Thus, compounds that promote the interactions of these stimulatory molecules of c-ret would enhance the activity of c-ret. Alternatively, protein phosphatases can remove the phosphoryl moieties

placed on the intracellular region of c-ret in response to GDNF, and thus inhibit the signaling capability of c-ret. Thus compounds that inhibit phosphatases of c-ret will enhance the signaling capacity of c-ret. In the context of the present invention, the c-ret protein kinase could be activated by indolinone compounds that are modified with substituents, particularly at the 5 position of the oxindole ring.

c-ret is implicated in the development and survival

of enteric, synaptic, and sensory neurons and neurons of
the renal system upon stimulation by GDNF. Lack of
function mutations in c-ret can lead to Hirschsprung's
disease, for example, which manifests itself as a decrease
in intestinal tract innervation in patients. Thus,

compounds that activate c-ret are potential therapeutic
agents for the treatment of neurodegenerative disorders,
including, but not limited to, Hirschsprung's disease,
Parkinson's disease, Alzheimer's disease, and amyotrophic
lateral sclerosis. Compounds that inhibit c-ret function
are possible anti-cancer agents as over-expression of ret
in cells is implicated in cancers, such as cancer of the
thyroid.

Pharmaceutical Compositions and Administration of Indoli-25 none Compounds

Methods of preparing pharmaceutical formulations of the compounds, methods of determining the amounts of compounds to be administered to a patient, and modes of administering compounds to an organism are disclosed in 30 International Patent Publication No. WO 96/22976, published August 1, 1996 by Ballinari et al., which is incorporated herein by reference in its entirety, including any drawings. Those skilled in the art will appreciate that such descriptions are applicable to the present

57

invention and can be easily adapted to it. The mechanism of such action and possible uses for such compounds are described in International Patent Publication WO 96/40116, published December 19, 1996 by Tang et al.

The compounds described herein can be administered to a human patient per se, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition or in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

15 Effective Dosage

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an amount effective to achieve its intended purpose. More specifically, a 20 therapeutically effective amount means an amount of compound effective to prevent, alleviate or ameliorate symptoms of disease or prolong the survival of the subject being treated. Determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein and in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

30 Packaging

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient according to the description provided in International Patent

58

Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

Examples

The examples below are not limiting and are merely representative of various aspects and features of the present invention. The examples demonstrate methods of synthesizing indolinone compounds of the invention. The examples also demonstrate the specificity as well as the potency with which these compounds inhibit protein kinase function in cells.

Example 1: Compound Synthesis

The compounds of the present invention may be synthesized according to known techniques such as those described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al. The following represent preferred methods for synthesizing the compounds of the claimed invention.

(a) Preparation of 4-Methyl-2-oxindole. Diethyl oxalate (30 mL) in 20 mL of dry ether was added with stirring to 19 g of potassium ethoxide suspended in 50 mL of dry ether. The mixture was cooled in an ice bath and 20 mL of 3-nitro-o-xylene in 20 mL of dry ether was slowly added. The thick dark red mixture was heated to reflux for 0.5 hr, concentrated to a dark red solid, and treated with 10% sodium hydroxide until almost all of the solid dissolved. The dark red mixture was treated with 30% hydrogen peroxide until the red color changed to yellow. The mixture was treated alternatively with 10% sodium hydroxide and 30% hydrogen peroxide until the dark color was no longer present. The solid was filtered off and the

filtrate acidified with 6N hydrochloric acid. The resulting precipitate was collected by vacuum filtration, washed with water, and dried under vacuum to give 9.8 g (45% yield) of 1-methyl-6-nitrophenylacetic acid as an off-white solid. The sold was hydrogenated in methanol over 10% palladium on carbon to give 9.04 g of the title compound as a white solid.

- (b) Preparation of 5-Nitro-2-oxindole. The 210 oxindole (6.5 g) was dissolved in 25 mL of concentrated sulfuric acid and the mixture maintained at -10 -15 °C while 2.1 mL of fuming nitric acid was added dropwise. After the addition of the nitric acid the reaction mixture was stirred at 0°C for 0.5 hr and poured into ice water.
- The precipitate was collected by filtration, washed with water and crystallized from 50% of the acetic acid. The final crystal was then filtered, washed with water and dried under vacuum to give 6.3g (70%) of 5-nitro-2-oxindole.

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(c) Preparation of 5-Amino-2-oxindole. The 5-nitro-2-oxindole (6.3 g) was hydrogenated in methanol over 10% palladium on carbon to give 3.0 g (60% yield) of the title compound as a white solid.

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- (d) Preparation of 5-Fluoro-2-oxindole. 5-Fluoroi-satin (8.2 g) was dissolved in 50 mL of hydrazine hydrate and refluxed for 1 hr. The reaction mixtures were then poured in ice water. The precipitate was then filtered, washed with water and dried under vacuum oven to give 6.0 g of 5-fluoro-2-oxindole (79% yield).
 - (e) Preparation of 5-Bromo-2-oxindole. 2-Oxindole (1.3 g) in 20 mL of acetonitrile was cooled to -10 $^{\circ}$ C and

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2.0 g of N-bromosuccinimide was slowly added with stirring. The reaction was stirred for 1 hour at -10°C and 2 hours at 0°C. The precipitate was collected, washed with water and dried to give 1.9 g (90% yield) of the title 5 compound.

(f) Preparation 5-Carboxy-2-oxindole

Step 1. Synthesis of 5-Methoxycarbonyl-2oxindole. 5-Iodo-2-oxindole (17g) was refluxed with 2g of 10 palladium diacetate, 18.15g of triethylamine, 150 mL of methanol, 15 mL of dimethylsulfoxide and 2.6 g of DPPP in an atmosphere saturated with carbon monoxide. After 24 hours, the reaction was filtered to remove the catalyst and the filtrate concentrated. The concentrate was 15 chromatographed on a silica gel in 30% ethyl acetate in The fractions containing product were concenhexane. trated and allowed to stand. The precipitated product was collected by vacuum filtration to give 0.8g (7%) of the title compound as an off-white solid.

Step 2: Synthesis of 5-Carboxy-2-oxindole. Methoxycarbonyl-2-oxindole (1g) and 1g of sodium hydroxide in 20 mL of methanol was refluxed for 3 hours. reaction mixture was cooled and concentrated to dryness. The residue was dissolved in water and extracted twice 25 with ethyl acetate. The aqueous layer was acidified with 6 N hydrochloric acid and the precipitated solid collected, washed with water, and dried to give 0.7g (78%) of the title compound as an off-white solid.

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30 (g) Preparation of 5-Carboxyethyl-2-oxindole Step 1: Synthesis of 5-Chloroacety1-2oxindole. Aluminum chloride (30.8 g) and 2-oxindole (5.0g) were added to 200 ml of carbon disulfide at room temperature and the mixture stirred. Chloroacetyl chloride (3.8 mL) was added and the stirring continued for 1 hour. The mixture was heated to reflux for 3 hours, cooled and the solvent decanted. The residue was stirred in ice water until it became a solid suspension. The solid was collected by vacuum filtration, washed in water, and dried to give 7.0g (90% yield) of the title compound.

Step 2: Synthesis of 5-Chloroethyl-2-oxindole. 5-Chloroacetyl-2-oxindole (7.0g) was added to 25 mL of trifluoroacetic acid and the mixture cooled in an ice bath with stirring. Triethylsilane (12.3 mL) was added dropwise over 2 minutes. The reaction was then stirred at room temperature for 4 hours and poured into ice water. Hexane was added, the mixture stirred vigorously, and the solid collected by vacuum siltation and washed with hexane to give 5.9g (91% yield) of the product as a white solid.

Step 3: Synthesis of 5-Cyanoethyl-2-oxindole. Potassium cyanide (2.02 g) was added to 15 mL of dimethylsulfoxide and heated to 90°C 5-Chloroethyl-2-oxindole (3.0 g) dissolved in 5mL of dimethylsulfoxide was added slowly with stirring, and the reaction heated to 150°C for 2 hours. The mixture was cooled, poured into ice water and the precipitate collected by vacuum filtration, washed with water, and dried to give crude product. The crude material was chromatographed on silica gel in 5% methanol in chloroform to give 1.2g (42% yield) of the title compound.

Step 4: Synthesis of 5-Carboxyethyl-2-oxindole. 5-Cyanoethyl-2-oxindole (4.02g) in 10mL of water containing 25mL of concentrated hydrochloric acid was refluxed for 4 hours. The mixture was cooled, water added and the resulting solid collected by vacuum filtration, washed with water and dried to give 1.9g (44% yield) of the title compound as a yellow solid.

62

(h) Preparation of 3,5-Dimethylpyrrol-2-carboxaldehyde

5-Cyanoethly-2-oxindole (4.02g) in 10 mL of water containing 25mL of concentrated hydrochloric acid was refluxed for 4 hours. The mixture was cooled, water added and the resulting solid collected by vacuum filtration, washed with water and dried to give 1.9g (44% yield) of the title compound as a yellow solid.

(i) Preparation of 3,5-Dimethylpyrrol-2-carboaldehyde

To a solution dimethylformamide (80.4g) and 1L of dichloroethane at 0°C was added phosphorous oxychoride (153.3q) over a few minutes and the reaction stirred for 15 1-2 hr at 0° C 2,4-Dimethylpyrrole (114.6g) was added dropwise to the above solution at temperature below 5°C. After the addition was complete the reaction was heated and the aqueous layer isolated and saved. The organic layer was extracted again with 300mL of water and the two 20 aqueous layers combined. The aqueous phase was extracted with 200mL of dichloroethane and the organic layer discarded. The aqueous phase was cooled to 10°C and adjusted to pH 10 with 10% sodium hydroxide. The mixture was stirred at 10°C for 2hr. The yellow solid was collected 25 by vacuum filtration and washed thoroughly with water. The solid was dried at room temperature under vacuum to give 110.8g (90% yield of 2,4-dimethyl-5-formylpyrrole.

(j) Preparation of 3,5-Diethylpyrrol-2-carboxal-30 dehyde:

The solution of 25.0g of 3,5-heptanedione and 42.3g of diethyl aminomalonate hydrochloride in 200 mL of acetic acid was heated to 95- 10° C for 1.25 hr. Sodium acetate was added and the reaction mixture was stirred for 5.35 hr

63

and cooled down for 4 hr. The salt was filtered and washed with acetic acid. The acetic acid solution was then concentrated and the residue poured into 800 mL of water. The yellow solid was filtered and dried in a vacuum oven overnight to give 36.0g of ethyl 3,5-diethlypyrrol-2-carboxalate as the orange liquid (92% yield).

Decarboxylation of ethyl 3,5-diethylpyrro-2-carboxalate upon hydrolysis gave 2,4-diethylpyrrole. The title 10 compound was then synthesized via Vilsmeier formulation of 2,4-diethlpyrrole with the same condition used for the preparation of 3,5-dimethylpyrrol-5-carboxaldehyde.

(k) Preparation of 3,5-Diisopropylpyrrol-2-carboxal15 dehyde

The procedure was the same as the one for the preparation of 3,5-diethylpyrrol-2-carboxaldehyde except starting with 2,6-dimethyl-3,5-heptanedione.

20 Example 2: FLK Inhibition by Indolinone compounds of the Invention

An enzyme linked immunosorbent assay (ELISA) was conducted to measure the catalytic activity of the FLK-1 receptor and more specifically, the inhibition or activation of indolinone compounds on the catalytic activity of the FLK-1 receptor. Specifically, the following assay was conducted to measure catalytic activity of the FLK-1 receptor in FLK-1/NIH3T3 cells.

The materials and protocol for the FLK-1 ELISA assay
30 are as described in International Patent Publication No.
WO 96/40116, published December 19, 1996 by Tang et al.

Selected compounds were tested in the FLK-1 ELISA assay. IC50 measurements are reported in the tables. Derivatives of 3-[(indole-3-yl)methylene]-2-indolinone

64

compounds with a methyl substituent at the 1' position proved to be the most potent inhibitors of the group of compounds tested in the assay.

5 Example 3: In Vitro RTK Assays

The following in vitro assays may be used to determine the level of activity and effect of the different compounds of the present invention on one or more of the RTKs. Similar assays can be designed along the same lines for any tyrosine kinase using techniques well known in the art.

(a) Enzyme Linked Immunosorbent Assay (ELISA)

Enzyme linked immunosorbent assays (ELISA) may be used to detect and measure the presence of tyrosine kinase activity. The ELISA may be conducted according to known protocols which are described in, for example, Voller, et al., 1980, "Enzyme-Linked Immunosorbent Assay," In: Manual of Clinical Immunology, 2d ed., edited by Rose and Fried-20 man, pp 359-371 Am. Soc. Of Microbiology, Washington, D.C.

The disclosed protocol may be adapted for determining activity with respect to a specific RTK. For example, the preferred protocols for conducting the ELISA experiments for specific RTKs is provided below. Adaptation of these protocols for determining a compound's activity for other members of the RTK family, as well as other receptor and non-receptor tyrosine kinases, are within the scope of those in the art.

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(i) FLK-1 ELISA

An ELISA assay was conducted to measure the kinase activity of the FLK-1 receptor and more specifically, the inhibition or activation of protein tyrosine kinase

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activity on the FLK-1 receptor. Specifically, the following assay was conducted to measure kinase activity of the FLK-1 receptor in FLK-1/NIH3T3 cells.

5 Materials And Methods.

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Materials. The following reagents and supplies were used:

- a. Corning 96-well ELISA plates (Corning Catalog No. 25805-96);
- b. Cappel goat anti-rabbit IgG (catalog no. 55641);
 - c. PBS (Gibco Catalog No. 450-1300EB);
- d. TBSW Buffer (50 mM Tris (pH 7.2), 150 mM NaCl and 0.1% Tween-20);
 - e. Ethanolamine stock (10% ethanolamine (pH 7.0), stored at $4^{\circ}C$);
- f. HNTG buffer (20mM HEPES buffer (pH 7.5), 150mM NaCl, 0.2% Triton X-100, and 10% glycerol);
 - g. EDTA (0.5 M (pH 7.0) as a 100X stock);
- h. Sodium ortho vanadate (0.5 M as a 100X stock);
 - i. Sodium pyro phosphate (0.2M as a 100X stock);
- j. NUNC 96 well V bottom polypropylene plates (Applied Scientific Catalog No. AS-72092);
 - k. NIH3T3 C7#3 Cells (FLK-1 expressing cells);

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1.	DMEM	with	1X	high	glucose	L	Glutamine	(catalog
	No. 11965-050);							

m. FBS, Gibco (catalog no. 16000-028);

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- n. L-glutamine, Gibco (catalog no. 25030-016);
- o. VEGF, PeproTech, Inc. (catalog no. 100-20) (kept as 1 μ g/100 μ l stock in Milli-Q dH₂O and stored at -20°C;
 - p. Affinity purified anti-FLK-1 antiserum which can be obtained or purified as follows:

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1. Prepare a Tresyl-Activated Agarose/Flk-1-D column by incubating 10 ml of Tresyl-Activated Agarose with 20 mg of purified GST-Flk-1-D fusion protein in 100mM sodium bicarbonate (pH 9.6) buffer overnight at 4oC.

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- 2. Wash the column once with PBS.
- 3. Block the excess sites on the column with 2 M glycine for 2 hours at 4oC.
- 4. Wash the column with PBS.

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- 5. Incubate the column with Rabbit anti-Flk-1D production bleed for 2 hours at 4oC.
- 6. Wash the column with PBS.
- 7. Elute antiserum with 100 mM Citric Acid, pH3.0 and neutralize the eluate immediately with 2 M Tris, pH 9.0.

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8. Dialyize the eluate against PBS overnight at 4oC with 3 changes of buffer (sample to buffer ratio is 1:100).

- 9. Adjust the dialyized antiserum to 5% glycerol and store at -80oC in small aliquotes.
- 5 q. UB40 monoclonal antibody specific for phosphotyrosine, (see, Fendley, et al., 1990, Cancer Research 50:1550-1558);
- r. EIA grade Goat anti-mouse IgG-POD (BioRad cata-10 log no. 172-1011);
- s. 2,2-azino-bis(3-ethylbenz-thiazoline-6-sulfonic acid (ABTS) solution (100mM citric acid (anhydrous), 250 mM Na₂HPO₄ (pH 4.0), 0.5 mg/ml ABTS (Sigma catalog no. A-1888)), solution should be stored in dark at 4°C until ready for use;
 - t. H_2O_2 (30% solution) (Fisher catalog no. H325);
- 20. u. ABTS/ H_2O_2 (15ml ABTS solution, 2 μ l H_2O_2) prepared 5 minutes before use and left at room temperature;
 - v. 0.2 M HCl stock in H_2O ;

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- w. dimethylsulfoxide (100%) (Sigma Catalog No. D-8418); and
- x. Trypsin-EDTA (Gibco BRL Catalog No. 25200-049).
 30 Protocol. The following protocol was used for conducting the assay:
 - 1. Coat Corning 96-well elisa plates with 1.0 μ g per well Cappel Anti-rabbit IgG antibody in 0.1M Na₂CO₃ pH 9.6. Bring final volume to 150 μ l per well. Coat plates

overnight at 4°C . Plates can be kept up to two weeks when stored at 4°C .

- 2. Grow cells in Growth media(DMEM, supplemental with 2.0mM L-Glutamine, 10% FBS) in suitable culture dishes until confluent at 37°C, 5% CO₂.
 - 3. Harvest cells by trypsinization and seed in Corning 25850 polystyrene 96-well roundbottom cell plates, 25.000 cells/well in 200µl of growth media.
 - 4. Grow cells at least one day at 37° C, 5% CO₂.
- 10 5. Wash cells with D-PBS 1X.
 - 6. Add 200 μ l/well of starvation media (DMEM, 2.0mM l-Glutamine, 0.1% FBS). Incubate overnight at 37°C, 5% CO₂.
- 7. Dilute Compounds/Extracts 1:20 in polypropylene
 15 96 well plates using starvation media. Dilute dimethylsulfoxide 1:20 for use in control wells.
 - 8. Remove starvation media from 96 well cell culture plates and add 162 μl of fresh starvation media to each well.
- 9. Add 18µl of 1:20 diluted Compound/Extract dilution (from step 7) to each well plus the 1:20 dimethylsulfoxide dilution to the control wells (+/-VEGF), for a final dilution of 1:200 after cell stimulation. Final dimethylsulfoxide is 0.5 %. Incubate the plate at 37°C, 5% CO₂ for two hours.
 - 10. Remove unbound antibody from ELISA plates by inverting plate to remove liquid. Wash 3 times with TBSW + 0.5% ethanolamine, pH 7.0. Pat the plate on a paper towel to remove excess liquid and bubbles.
- 11. Block plates with TBSW + 0.5% Ethanolamine, pH 7.0, 150 µl per well. Incubate plate thirty minutes while shaking on a microtiter plate shaker.
 - 12. Wash plate 3 times as described in step 10.

minutes.

- 13. Add $0.5\mu g/well$ affinity purified anti-FLU-1 polyclonal rabbit antiserum. Bring final volume to $150\mu l/well$ with TBSW + 0.5% ethanolamine pH 7.0. Incubate plate for thirty minutes while shaking.
- 5 14. Add 180 μ l starvation medium to the cells and stimulate cells with 20 μ l/well 10.0mM sodium ortho vanadate and 500 ng/ml VEGF (resulting in a final concentration of 1.0mM sodium ortho vanadate and 50ng/ml VEGF per well) for eight minutes at 37°C, 5% CO₂. Negative control wells receive only starvation medium.
 - 15. After eight minutes, media should be removed from the cells and washed one time with 200µl/well PBS.
 - 16. Lyse cells in 150µl/well HNTG while shaking at room temperature for five minutes. HNTG formulation includes sodium ortho vanadate, sodium pyro phosphate and EDTA.
 - 17. Wash ELISA plate three times as described in step 10.
- 18. Transfer cell lysates from the cell plate to elisa plate and incubate while shaking for two hours. To transfer cell lysate pipette up and down while scrapping the wells.
 - 19. Wash plate three times as described in step 10.
- 20. Incubate ELISA plate with 0.02µg/well UB40 in TBSW + 05% ethanolamine. Bring final volume to 150µl/well. Incubate while shaking for 30 minutes.
 - 21. Wash plate three times as described in step 10.
- 22. Incubate ELISA plate with 1:10,000 diluted EIA grade goat anti-mouse IgG conjugated horseradish peroxi30 dase in TBSW + 0.5% ethanolamine, pH 7.0. Bring final volume to 150µl/well. Incubate while shaking for thirty
 - 23. Wash plate as described in step 10.

70

- $24.~\text{Add}~100~\text{µl}~\text{of}~\text{ABTS/H}_2\text{O}_2$ solution to well. Incubate ten minutes while shaking.
- 25. Add 100 µl of 0.2 M HCl for 0.1 M HCl final to stop the color development reaction. Shake 1 minute at room temperature. Remove bubbles with slow stream of air and read the ELISA plate in an ELISA plate reader at 410 nm.

(ii) HER-2 ELISA

HER-2 ELISA assays are described in International 10 Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

(iii) PDGF-R ELISA

A PDGF-R ELISA is described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

(iv) IGF-I ELISA

The IGF-I ELISA protocol described in International 20 Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al. may be used to measure phosphotyrosine level on IGF-I receptor, which indicates IGF-I receptor tyrosine kinase activity.

25 (v) EGF Receptor ELISA

EGF Receptor kinase activity (EGFR-NIH3T3 assay) in whole cells was measured as described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

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(vi) Cellular Insulin Receptor ELISA

The protocol described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al. was used to determine whether the compounds

WO 98/07695

71

of the present invention possessed insulin receptor tyrosine kinase activity.

(vii) EGFR ELISA ASSAY

5 Purpose

To provide a consistent method for measuring the in vitro kinase activity of the EGFR in an Enzyme-linked immunosorbent assay (Elisa).

Scope. The following protocol describes the procedures used to analyze protein tyrosine kinase activity on the EGFR in an Elisa. The procedure also describes the protocol for the initial screening of drugs for inhibition or activation of protein tyrosine kinase activity.

Reagents and Supplies.

- 1. Corning 96-well Elisa plates
 Corning Catalog #25805-96
 - 2. 05-101 monoclonal anti-EGFR antibody (commercially available from UB1)

-80° C, 1 ml aliquots

20 3. PBS (Dulbecco's Phosphate-Buffered Saline)
Gibco Catalog # 450-1300EB

Formulation: 2.7 mM KCL

1.1 mM KH2PO.

0.5 mM MgCl₂ (anhydrous)

25 138 mM NaCl

8.1 mM Na2HPO.

4. TBST Buffer

Formulation: 50 mM Tris pH 7.2

150 mM NaCl

30 0.1% Triton X-100

5. Blocking Buffer

Formulation: 5% Carnation Instant Milk in PBS

6. A431 cell lysate

72

A431 cells are available from a variety of commercial sources and may be used lysed using conventional methods known to those skilled in the art or as described for lysis of the 3T3 cells in the EGF cellular assay described herein. -80° C, 1 ml aliquots

7. TBS Buffer

Formulation: 50 mM Tris pH 7.2

150 mM NaCl

8. TBS + 10% DMSO

10 Formulation: 10% DMSO in TBS Buffer

(DMSO from Sigma, Catalog # D-2650)

9. ATP/MnCl₂ phosphorylation mix

Formulation: 0.03 mM ATP

(Adenosine-5'-triphosphate, Sigma Catalog

15 #A-5394)

50 mM MnCl,

Make fresh in autoclaved Milli-Q H2O immediately before use

Keep on ice until use

- 20 10. NUNC 96-well V bottom polypropylene plates Applied Scientific Catalog # AS-72092
 - 11. EDTA

Formulation: 200 mM EDTA pH 8.0

- 12. Rabbit polyclonal anti-phosphotyrosine serum or
 UB40 monoclonal antibody specific for phosphotyrosine or
 UBI's mab 4610, Upstate Biotechnology, Lake Placid, New
 York, Catalog # 05-321
 - 80° C, 1 ml aliquots

Thaw 1 ml vial and aliquot in smaller volumes to

30 store at - 80° C

 $\label{eq:Antiserum is stable for weeks when thawed and stored at 4 <math display="inline">\ensuremath{\text{C}}$

13. Goat anti-rabbit IgG peroxidase conjugate Biosource Catalog # ALIO404

73

14. ABTS Solution

Formulation: 100 mM Citric Acid (anhydrous)

250 mM Na₂HPO4 pH 4.0

0.5 mg/ml ABTS

5 (2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid)

(Sigma Catalog # A-1888)

Keep solution in dark at 4 C until ready to use

- 15. Hydrogen peroxide 30% solution
- 10 Fisher Catalog # H325

 Store in the dark at 4 C until ready to use
 - 16. ABTS/H₂O₂

Formulation: 15 mls ABTS solution

2 ul H₂O₂

Prepare 5 minutes before use and room temperature

- 17. 0.2 M HCL stock in H_2O Procedure.
- 1. Coat Corning 96-well elisa plates with 0.5 ug 20 per well 05-101 antibody.

Bring final volume to 100 ul per well with PBS. Coat plates overnight at 4° C.

- 2. Remove unbound 05-101 from wells by inverting plate to remove liquid.
- 25 Wash 1x with distilled H2O by filling wells
 Pat the plate on a paper towel to remove excess
 liquid.
 - Block plates with 5% milk in PBS.
 150 ul per well.
- Incubate plate 30 minutes while shaking on a microtiter plate shaker.
 - 4. Wash plate 3x with dionized water, then once with TBST

74

5. Add 7 ug A431 cell lysate per well (EGFR source).

Add PBS to final volume of 100 ul per well Incubate 30 minutes while shaking.

- 5 6. Wash as described in step 4.
 - 7. At this point, drugs or extracts are added to the wells.

Dilute drugs/extracts 1:100 (unless specified otherwise) in TBS + 10% DMSO in 96-well polypropylene 10 plates.

Add 120 ul TBS to ELISA plate containing captured EGFR.

Add 13.5 ul diluted drugs/extracts to ELISA plate.

To control wells (wells which do not receive any drug) add 135 ul TBS

+ 1% DMSO.

Incubate plate 30 minutes while shaking.

8. Add 15 ul of 0.03 mM ATP + 50 mM MnCl₂ phosphory-20. lation mix directly to all wells except negative control well which does not receive ATP/MnCl₂ (see diagram).

 $$(150\ ul\ final\ volume\ in\ well\ with\ 3\ uM\ ATP/5\ mM\ MnCl2\ final\ concentration\ in\ well.)$

Incubate 5 minutes while shaking vigorously.

25 *NOTE: It is critical that ATP/MnCl2

phosphorylates the receptor for 5 minutes only. It is best to add the ATP/MnCl₂ with an 12 channel pipettor 1 row at a time leaving 20 seconds between each row so that the reaction may be stopped with EDTA exactly 5 minutes later (this depends on the number of plates being phosphorylated in one batch). Shake between each addition.

9. After 5 minutes, to stop reaction, add 16.5 ul of 200 mM EDTA pH 8.0 for 20 mM final in well, shaking

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continuously between each addition. This is done using the same timing method as above. After last row has received EDTA, shake plate an additional minute.

- 10. Wash 4x with deionized water, twice with TBST.
- 5 11. Add rabbit polyclonal anti-phosphotyrosine serum.

Dilute 1:3000 in TBST.

Add 100 ul per well.

Incubate 30-45 minutes while shaking.

- 10. 12. Wash as described above in step 4.
 - 13. Add BioSource anti-rabbit peroxidase conjugate antibody.

Dilute 1:2000 in TBST.

Add 100 ul per well.

- 15 Incubate 30 minutes while shaking.
 - 14. Wash as described in step 4.
 - 15. Add 100 ul of $ABTS/H_2O_2$ solution to well. Incubate 5 to 10 minutes while shaking. Remove bubbles
- 20 16. If necessary stop reaction with the addition of 100ul of 0.2M HCl per well
 - 17. Read assay on Dynatech MR7000 elisa reader.

Test Filter: 410 nM

Reference Filter: 630 nM

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(b) Cell Growth Assays

The cell growth assays described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al. may be conducted to measure the effect of the claimed compounds upon cell growth as a result of the compound's interaction with one or more RTKs.

(vi) Assay Measuring Phosphorylating Function of Raf

The following assay reports the amount of RAF-catalyzed phosphorylation of its target protein MEK as well as MEK's target MAPK. The RAF gene sequence is described in Bonner et al., 1985, Molec. Cell. Biol. 5: 1400-1407, and is readily accessible in multiple gene sequence data banks. Construction of the nucleic acid vector and cell lines utilized for this portion of the invention are fully described in Morrison et al., 1988, Proc. Natl. Acad. Sci. USA 85: 8855-8859.

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Materials and Reagents

- 1. Sf9 (Spodoptera frugiperda) cells; GIBCO-BRL, Gaithersburg, MD.
- RIPA buffer: 20 mM Tris/HCl pH 7.4, 137 mM NaCl,
 10 % glycerol, 1 mM PMSF, 5 mg/L Aprotenin, 0.5 % Triton X-100;
 - 3. Thioredoxin-MEK fusion protein (T-MEK): T-MEK expression and purification by affinity chromatography were performed according to the manufacturer's procedures.
- 20 Catalog# K 350-01 and R 350-40, Invitrogen Corp., San Diego, CA
 - 4. His-MAPK (ERK 2); His-tagged MAPK was expressed in XL1 Blue cells transformed with pUC18 vector encoding His-MAPK. His-MAPK was purified by Ni-affinity chromatog-
- 25 raphy. Cat# 27-4949-01, Pharmacia, Alameda, CA
 - 5. Sheep anti mouse IgG: Jackson laboratories, West Grove, PA Catalog, # 515-006-008, Lot# 28563
 - RAF-1 protein kinase specific antibody: URP2653 from UBI.
- 7. Coating buffer: PBS; phosphate buffered saline, GIBCO-BRL, Gaithersburg, MD
 - 8. Wash buffer: TBST 50 mM Tris/HCL pH 7.2, 150 mM NaCl, 0.1 % Triton X-100
 - 9. Block buffer: TBST, 0.1 % ethanolamine pH 7.4

- 10. DMSO, Sigma, St. Louis, MO
- 11. Kinase buffer (KB): 20 mM Hepes/HCl pH 7.2, 150 mM NaCl, 0.1 % Triton X-100, 1 mM PMSF, 5 mg/L Aprotenin, 75 μ M sodium ortho vanadate, 0.5 mM DTT and 10 mM MgCl₂.
- 5 12. ATP mix: 100 mM MgCl₂, 300 μ M ATP, 10 μ Ci γ -³³P ATP (Dupont-NEN)/mL.
 - 13. Stop solution: 1 % phosphoric acid; Fisher, Pittsburgh, PA.
- 14. Wallac Cellulose Phosphate Filter mats; Wallac,10 Turku, Finland.
 - 15. Filter wash solution: 1 % phosphoric acid, Fisher, Pittsburgh, PA.
 - 16. Tomtec plate harvester, Wallac, Turku, Finland.
- 17. Wallac beta plate reader # 1205, Wallac, Turku, 15 Finland.
 - 18. NUNC 96-well V bottom polypropylene plates for compounds Applied Scientific Catalog # AS-72092.

Procedure

- All of the following steps are conducted at room temperature unless specifically indicated.
 - 1. ELISA plate coating: ELISA wells are coated with 100 μ L of Sheep anti mouse affinity purified antiserum (lµg/100 μ L coating buffer) over night at 4 °C. ELISA plates can be used for two weeks when stored at 4 °C.
 - 2. Invert the plate and remove liquid. Add 100 μL of blocking solution and incubate for 30 min.
 - 3. Remove blocking solution and wash four times with wash buffer. Pat the plate on a paper towel to remove excess liquid.
 - 4. Add 1 μg of purified Sumo 22 to each well and incubate for 1 hour. Wash as described in step 3.
 - 5. Thaw lysates from RAS/RAF infected Sf9 cells and dilute with TBST to 10 $\mu g/100~\mu L$. Add 10 μg of diluted

lysate to the wells and incubate for 1 hour. Shake the plate during incubation. Negative controls receive no lysate. Lysates from RAS/RAF infected Sf9 insect cells are prepared after cells are infected with recombinant 5 baculoviruses at a MOI of 5 for each virus, and harvested 48 hours later. The cells are washed once with PBS and lysed in RIPA buffer. Insoluble material is removed by centrifugation (5 min at 10 000 \times g). Aliquots of lysates are frozen in dry ice/ethanol and stored at - 80 °C until use.

6. Remove non-bound material and wash as outlined above (step 3).

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- Add 2 μg of T-MEK and 2 μg of His-MAPK per well and adjust the volume to 40 µL with kinase buffer.
- Predilute compounds (stock solution 10 mg/mL 15 DMSO) or extracts 20 fold in TBST plus 1% DMSO. Add 5 µL of the prediluted compounds/extracts to the wells described in step 6. Incubate for 20 min. Controls receive no drug.
- 20 Start the kinase reaction by addition of 5 μL ATP mix; Shake the plates on an ELISA plate shaker during incubation.
 - 10. Stop the kinase reaction after 60 min by addition of 30 µL stop solution to each well.
- 25 Place the phosphocellulose mat and the ELISA plate in the Tomtec plate harvestor. Harvest and wash the filter with the filter wash solution according to the manufacturers recommendation. Dry the filter mats. the filter mats and place them in the holder. Insert the 30 holder into radioactive detection apparatus and quantitate the radioactive phosphorous on the filter mats.

Alternatively, 40 µL aliquots from individual wells of the assay plate can be transferred to the corresponding positions on the phosphocellulose filter mat. After air-

79

drying the filters, put the filters in a tray. Gently rock the tray, changing the wash solution at 15 min intervals for 1 hour. Air-dry the filter mats. Seal the filter mats and place them in a holder suitable for measuring the radioactive phosphorous in the samples. Insert the holder into a detection device and quantitate the radioactive phosphorous on the filter mats.

(c) Toxicity and Animal Models

Measurement Of Cell Toxicity and *In Vivo* Animal Models are described in International Patent Publication No. WO 96/40116, published December 19, 1996 by Tang et al.

(d) MET Biochemical Kinase Assay

A met biochemical kinase assay may be performed for 15 met generally as described above for other kinases by substituting that or the other kinases. In particular, ELISA plates are coated with goat anti-rabbit Fc antibodies, which are used to capture commercially available 20 (from Santa Cruz Biotechnology) rabbit polyclonal antibodies to the cytoplasmic domain of human MET. Lysates are from 293T cells that have been transiently transfected with a chimeric receptor composed of the extracellular domain of the EGFr and the transmembrane and 25 cytoplasmic domain of the MET receptor, or from NCI-H441 cells (a human lung adenocarcinoma cell line) which express high endogenous levels of MET. The chimeric receptors, or MET, from these lysates are captured on the antibody coated plates. After washing away extraneous 30 proteins, test compounds are added and an in vitro kinase assay is performed by addition of an appropriate kinase buffer (containing ATP, divalent metal ions, etc.). Incorporation of phosphate into the captured receptors is detected with an anti-phosphotyrosine antibody conjugate

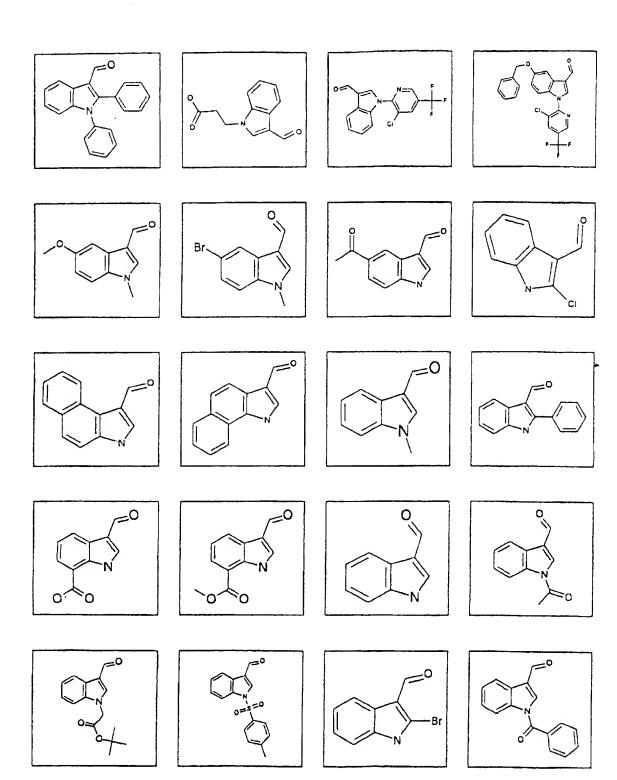
80

with horse radish peroxidase using TMB as a substrate for colorimetric detection.

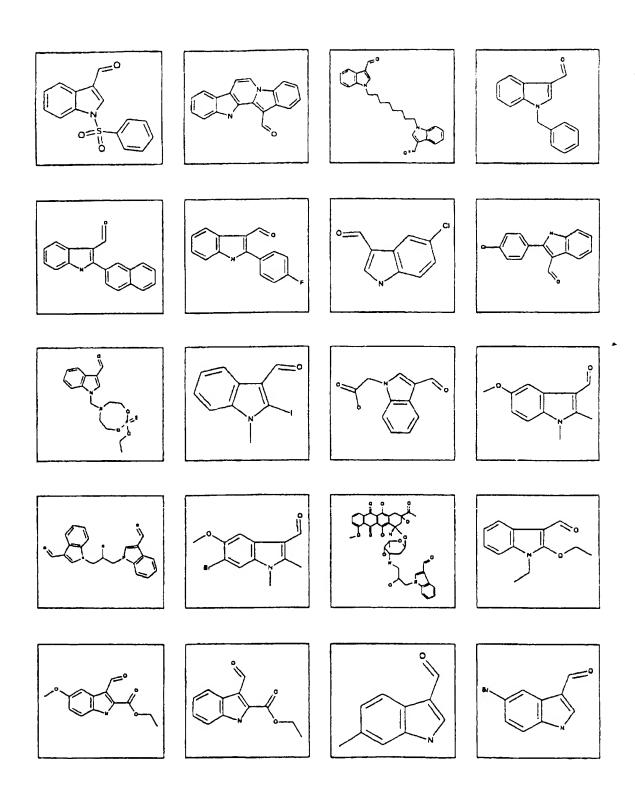
The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

All references cited herein are hereby incorporated by reference in their entirety.

Other embodiments are within the following claims.



Page 1



Page 2

Table 1, Sheet 3 of 3

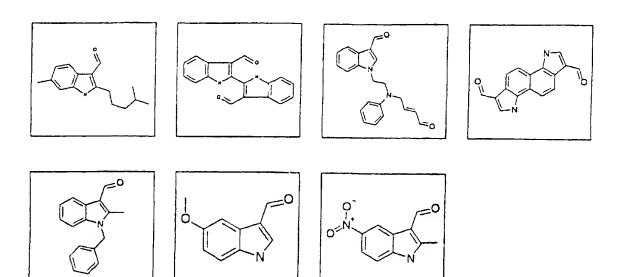


TABLE 2

FLK Kinase	STRUCTURES
IC50 (μM)	
0.7	1
	CINO N
7.7	I C
2.5	
14	F N
13	H N

TABLE 3, SHEET 1 OF 3

NUMBER	D	STRUCTURE
1 .	ind/ald-001	**************************************
2	ind/ald-002	CH,
3	ind/ald-003	
4	ind/ald-004	
5	ind/ald-005	
6	ind/ald-006	o ch
_	ind/ald-007	
8	ind/ald-008	
9	ind/ald-009	र के र
1 0.	ind/ald-010	
11	ind/ald-011	H,C-°

TABLE 3, SHEET 2 OF 3

12	ind/ald-012
1 3	ind/ald-013
1 4	ind/ald-014
15	ind/ald-015 *** Ch
16	ind/ald-016 mc-0 cm,
17	ind/ald-017
18	ind/ald-018
19	ind/ald-019
20	ind/ald-020
21	ind/ald-021
22	ind/ald-022
23	ind/ald-023

TABLE 3, SHEET 3 OF 3

24	ind/ald-024
25	ind/ald-025

TABLE 4, SHEEL 1 OF 3

NUMBER	CORP ID	STRUCTURE
1	oxindole-001	H N
2	oxindole-002	Br
3	oxindole-003	CI
4	oxindole-004	H.C. CHI
5	oxindole-005	ÇN.
6	oxindole-006	0
7	oxindol ← 007	CII,
8	oxindole-008	Br O
9	oxindole-009	CI
10	oxindole-010	F_O
1 1	oxindole-011	

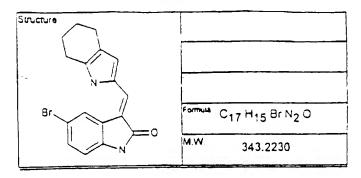
TABLE 4, SHEET 2 OF 3

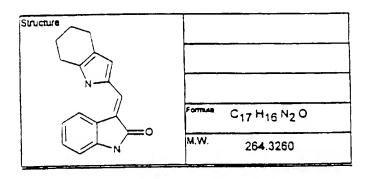
12	oxindole-012	, No o
13	oxindole-013	CI
14	oxindole-014	H,C O
15	oxindole-015	Br O
16	oxindole-016	F
17	cxindole-028	но СН,
18	oxindole-036	H _M N ^S O
19	oxindole-037	H.C., S
20	oxindole-038	, L Ro
21	oxindole-039	P.O.
22	oxindole-040	
23	oxindole-041	G C

TABLE 4. SHEEL 3 OF 3

24	oxindole-045	H.C.
25	oxiadole-048	но
26	oxindole-050	
27	oxiadole-054	CH ₃
28	oxindole-056	**************************************
29	oxindole-057	H¹C O
30	oxindole-058	H ₂ C N
31	oxindole-059	
32	; oxindole-060	1400
33	oxindole-061	
34	oxindole-062	H ₃ C O

TABLE 5





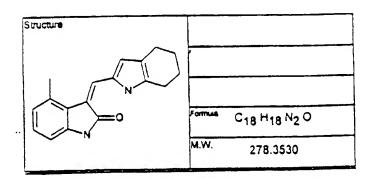
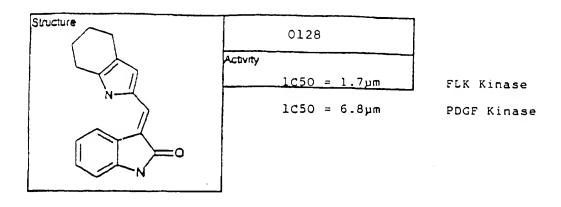


TABLE 6

FLK Kinase IC50 (µM)	STRUCTURES
1.2	
1.4	The state of the s
5	

TABLE 7



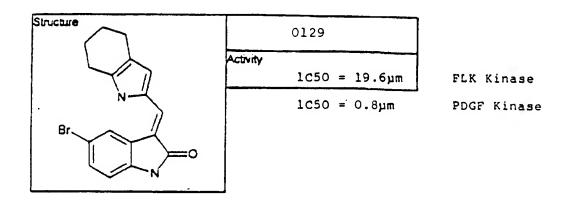
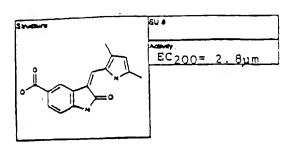
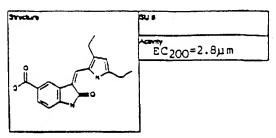
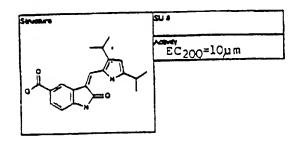
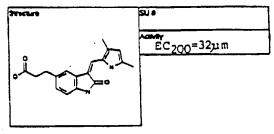


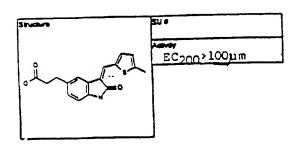
TABLE 8











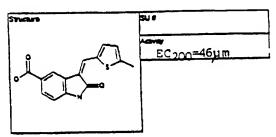


TABLE 9 (SHEET 1 OF 5)

	3-[(pyrrol-2-yl)methylidenyl]-5-sultonyl-2-indolinone
5	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-sulfonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-sulfonyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-sulfonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-sulfonyl-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]- 5-sulfonyl-2-indolinone
10	
•	3-[(pyrrol-2-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
15	3-[(3-methylthien-2-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-aminosulfonyl-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-methoxycarbonyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-methoxycarbonyl-2-indolinone
20	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-methoxycarbonyl-2-indolinon
	3-[(2-methylthien-5-yl)methylidenyl]-5-methoxycarbonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-methoxycarbonyl-2-indolinone
	3-{(4,5,6,7-tetrahydroindol-3-yl)methylidenyl}-5-methoxycarbonyl-2-indolinone
25	3-[(pyrrol-2-yl)methylidenyl]-5-diethanolamino-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-diethanolamino-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-diethanolamino-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-diethanolamino-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-diethanolamino-2-indolinone
30	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-diethanolamino-2-indolinone
	3-((ovrrol-2-vt)methylidenyl)-5-(2-3-dihydroxypropylamino)-2-indolinone

TABLE 9 (SHEET 2 OF 5)

5	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-(2,3-dihydroxypropylamino)-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-(2,3-dihydroxypropylamino)-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-(2,3-dihydroxypropylamino)-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-(2,3-dihydroxypropylamino)-2-indolinone
10	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-(2,3-dihydroxypropylamino)-2-
	3-[(pyrrol-2-yl)methylidenyl]-5-ureido-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-ureido-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-ureido-2-indolinone
15	3-[(2-methylthien-5-yl)methylidenyl]-5-ureido-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-ureido-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-ureido-2-indolinone
20	3-{(pyrrol-2-yl)methylidenyl]-5-guanidino-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-guanidino-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-guanidino-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-guanidino-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-guanidino-2-indolinone
25	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-guanidino-2-indolinone
	3-{(pyrrol-2-yl)methylidenyl]-5-glyceroylamido-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-glyceroylamido-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-glyceroylamido-2-indolinone
30	3-[(2-methylthien-5-yl)methylidenyl]-5-glyceroylamido-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-glyceroylamido-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-glyceroylamido-2-indolinone

TABLE 9 (SHEET 3 OF 5)

5	3-[(pyrrol-2-yl)methylidenyl]-5-[(3-piperldinyl)propanoylamino]-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-[(3-piperidinyl)propanoylamino]-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-[(3-piperidinyl)propanoylamino]-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-[(3-piperidinyl)propanoylamino]-2-indolinone
10	3-[(3-methylthien-2-yl)methylidenyl]-5-[(3-piperidinyl)propanoylamino]-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-[(3-pipendinyl)propanoylamino]-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-mesylamino-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-mesylamino-2-indolinone
15	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-mesylamino-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-mesylamino-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-mesylamino-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-mesylamino-2-indolinone
20	3-[(pyrrol-2-yl)methylidenyl]-5-glycoloyloxy-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-glycoloyloxy-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-glycoloyloxy-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-glycoloyloxy-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-glycoloyloxy-2-indollnone
25	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-glycoloyloxy-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinor
30	e
	3-[(2-methylthien-5-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinone

TABLE 9 (SHEET 4 OF 5)

	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-(2,3-dihydroxypropoxy)-2-indolinone
5	
	3-[(pyrrol-2-yl)methylidenyl]-5-aminomethyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-aminomethyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-aminomethyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-aminomethyl-2-indolinone
LO	3-[(3-methylthien-2-yl)methylidenyl]-5-aminomethyl-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-aminomethyl-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-amidino-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-amidino-2-indolinone
15	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-amidino-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-amidino-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-amidino-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-amidino-2-indolinone
20	3-[(pyrrol-2-yl)methylidenyl]-5-hydroxymethyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl] 5-hydroxymethyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl- 5-hydroxymethyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-hydroxymethyl-2-indolinone
	3-[(3-methy)thien-2-yt)methylidenyl]-5-hydroxymethyl-2-indolinone
25	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-hydroxymethyl-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-phosphonooxy-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-phosphonooxy-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-phosphonooxy-2-indolinone
30	3-[(2-methylthien-5-yl)methylidenyl]-5-phosphonooxy-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-phosphonooxy-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-phosphonooxy-2-Indolinone

TABLE 9 (SHEET 5 OF 5)

5	3-[(pyrrol-2-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
10	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-ethoxycarbonyl-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone
15	3-[(2-methylthien-5-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone 5-benzyloxycarbonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-benzyloxycarbonyl-2-indolinone
20	3-[(pyrrol-2-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
	3-{(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
	3-[(2-methylthien-5-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
25	3-[(4,5,6,7-tetrahydrolndol-3-yl)methylidenyl]-5-phenylaminocarbonyl-2-indolinone
	3-[(pyrrol-2-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone
	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone
	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone
30	3-[(2-methylthien-5-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone
	3-[(3-methylthien-2-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone
	3-[(4,5,6,7-tetrahydroindol-3-yl)methylidenyl]-5-benzylaminocarbonyl-2-indolinone

TABLE 10 SHEET 1 OF 5

FLK Kinase IC50 (μΜ)	STRUCTURES	METHOD
1.6	a C	A
2.6	T O N O	A
1.9	H Br Br	В
4.7		В
5.6	a The state of the	В
10.8		В
12.5		A

TABLE 10 SHEET 2 OF 5

		
0.97	The state of the s	В
1.5		В
1.1		В
3.5	The state of the s	A
7.3	THO NO	A
5.6	N O N	В
8.1		A
17.3		A

TABLE 10 SHEET 3 OF 5

2.9		В
5.2	CI NO Br	В
18.5	CH CO O O	В
8.8	a Br	В
4	1 0 0 × 1	В
8		B
11.5	and one	В
13.7	"Choo	В

TABLE 10 SHEET 4 OF 5

		-1
10.4		В .
10.7		В
16.4		В
19.9	the team	В
9.7	0,000	В
20.3	The contract of the contract o	В
4.6	THO N	В
5.6	a T N	В

TABLE 10 SHEET 5 OF 5

	11		
9.9		A	
12.3		В	
18.4	7000	В	
5.8		В	
6.2		Α .	
17.1		В	

Table 11

5-aminooxindele	slabnixoomord-2	5-chlorooxndole
oxindole-001	cxindole-002	oxindale-003
4,5-dimethyloxindale	5.5-dimethoxyoxindole	oxindae
oxingole-004	oxindole-005	czindole-006
4-methyloxindole	5,7-dibromooxindole	7-bromo-E-chlaroaxindale
oxindale-007	oxin dole_008	e009-slabnixo
5-fluorooxindole	5-nitrooxindole	5-iodooxindole
oxindale-010	oxindole-011	oxindale-012
		<u></u>
chloro-7-methyloxindale	5-methyloxindale	5-bramo-4-methyloxindole
oxindole-013	oxindole-014	oxindole-015
7-fluorooxindale	7-chlorooxindale	4-fluorooxindale

Table 11 (continued)

6-fluarooxin dale	4-chlorooxindale	3-chiarcaxindale
oxindale-019	cxindale-020	oxindoie-021
5-bromo-7-methyloxindale	7-chloro-5-cyanooxindole	4-bromooxindole
oxindcle-022	conixc	oxindole-024
7-methoxyoxindole	4-methyl-5-carboxyoxindole	4-methyl-5-carboxymethyloxind le
oxindole-025	oxincale-026	oxindale-027
-methyl-5-carboxyethyloxindole	4-methyl-5-(3-carboxy-n-propyl) oxindole	4-methyl-5-hydroxymethyloxind le
oxindole-028	oxindale-029	oxindole-030
4-methyl-5-methoxymethyloxind ole	4-methyl-5-(2-hydroxyethyl)oxin dole	4-methyl-5-(2-methoxyethyl)oxi dole
oxindole-031	oxindale-032	oxindole-033
4-methyl-5-(3-hydroxy-n-propyl) oxindole	4-methyl-5-(3-methoxy-n-propyl) oxindale	5-aminosulfonyloxIndole

Table 11 (continued

i-methylaminosulfonyloxindote	5-(4-influoromethylanilinosulfony l)oxindole	5-(morpholin-1-yl-sulfanyl)ox ale	
oxindale-037	exindale-038	oxndole-039	
6-trifluoromethyloxindole	5-(2-chlorœthyl)oxindole	5-carboxymethyloxindole	
oxindale-040	cxindale-041 axindale-042		
6-carboxymethyloxindole	4-methoxycarbonyloxindole	5-methoxycarbonyloxindo	
oxindale-043	oxindale-044 oxindale-0		
6-methoxycarbonyloxindole	4-carboxyoxindole	5-carboxyoxindcle	
6-methoxycarbonyloxindole oxindole-046	4-carboxyoxindole oxingole-047	5-carboxyoxindcle oxindole-048	
oxindale-046	oxindale-047	oxindole-048	
oxindale-046 6-carboxyoxindole	oxindole-047 5-carboxyethyloxindole	oxindole-048 5-hydroxyethyloxindole	
oxindale-046 6-carboxyoxindole	oxindole-047 5-carboxyethyloxindole	oxindole-048 5-hydroxyethyloxindole	

4-methyl-5-chlorcoxindole

oxindole-055

SSSD/22452. v01

Table 12

2-ethoxybenzaidenyde	2-thiopnenecarboxaldehyde	:-ताश्तागुराजुमाणीव-२-दवक्कव्यवावशागु de	
Ch:0-001	CHO-c02	CHO-103	
4-fluorobenzaldenyde	Inacie-3-carboxaldenyde	5-methyithrophene-2-carooxarde	
CHC-004	CHO-005	C3+;O-0C6	
4-bromobenzaldehyde	pyrrole-2-carboxalder.yde	2 Hydroxy-o-metroxypenzaiden yde	
CHC-307	CHO-008	C:+O-009	
J-metnyi-2-thiopnenecarboxalce hyde	3.4-Oibromo-s-metnyl-2-oyrroxed arboxaldenyde	Enyi-z. — Dimetryi- 5-formyi- J-py malecarooxytate	
CHO-010	CHO-011	CHO-012	
3-Brcmo-2-nydroxy-5-methoxyb enzaldehyde	1-Hydroxy-2-naphthaldenyde	Ethyl-2(ethoxycarbonyi)-4-(ethox ycarbonyimethyi)-5-lormyl-3-pym plapropionate	
CHO-013	CHO-014	CHO-015	
zihyi-5-iormyi-2-methyl-J-iuranci arboxylate	4-Formyi-3-metricycarbonymeth y1-5-me-1H-pyrrole-2-carboxytic acid methyl ester	2-Hydroxy-3-nitroterzaidehyde	
CHQ-016	CHO-017	CHO-018	
2.4-Dihydroxy-3-methylbenzalde lyde	Methyl5-rormyl-4-methy-3-pyrrol epropionate	2-furaldehyde	
CHO-019	CHO-020	CHO-021	
5-Nitro-2-furaldehyde	4-Ethoxy-3-methoxyoenzaldeny de	3,4-Dihydroxybenzaldehyde	
	}	CHO-024	

Table 12 (continued)

2,4-Oimethoxyoenzaldenyde	3,5-Ulmethyl-Lethyl-Z-pyrrolcar poraldehyde	2,4.6-Inmethoxybenzaldenyde	
CHC-025	CHC-128 CHO-027		
4-Hydroxydenzaldenyde	4-(Olmestylamino)-perizaidenyd e	2,4-Dimetryi-3-zaroethoxypyirol e-5-zaroxzkiehyde	
CHO-028	CHO-029	CHO-030	
2-chloro-4-flucrobenzaldeflyde	3-Nitrobertzaldehyde	4-riuarc-2-(Influoromethyl)oenz aldehyde	
CHC-031	CHO-03Z CHC-033		
2,4,6-Trifluoroberzaldehyde	4-riydroxy-2-methoxyperizaiden yde	3.4-Cimethoxybertzaldehyde	
сно-034	CHO-035	CHO-036	
Salicylaidehyde	Benzaldehyde	3, 5-dlethylpyrrole-2-carboxaldeh yde	
CHO-037	CHO-038	CHO-038	
5-(Methyithio)thicpnene-2-carbo xaldehyde	2.4-Oinyaraxy-o-matnyibenzaice hyde	Methyl-5-formyl-4-methyl-3-pym olepropionata	
CHO-039	CHO-040	CHO-041	
3-Ethoxy-4-hydroxypenzaldetryd e	2-Hydraxy-5-methaxybenzalden yde	2-Imidazolecarboxakiehyde	
CHO-042	CHO-043	CHO-044	
		· · · · · · · · · · · · · · · · · · ·	
1-Methyl-2-formylbenzimidazole	4-Chloro-1-methylpyrazoie-3-can boxaldehyde	2,3-dimethyl-5-formylthiophene	
CHO-045	CHO-046	CHO-046 CHO-047	

Table 12 (continued)

2-romyl-4, 5.6, 7-(e:ranydrainacl)	3-Chiorenethyi-3-nitrosalicyiald		
e	enyde (1-13.3-Dichicrochenyi)		
CHO-048	CHO-349	CHO-Æ0	
5-Chroretnicpnene-2-carocxaice hyde	3.5-dimethyl-5-formylpyrrole	ी-(-वेपर्ग-4-तेप्रवाच्यप्रवस्थावस्थापुर्व क	
CHC-051	CHO-35Z	C+C-053	
J-t-dutyl-3-oramo—1-nyaraxyoen	3.5-UH:ert-outyl-4-nydroxycenza	3-4-duty	
zaldenyde	Idenyde hemitydrate	Idahyde	
CHO-354	CHC-055 CHO-056		
2,4,3-Trihydroxybenzaldehyde	2-formyl-5-nitrathlophene	4-Carboxybenzaldehyde	
CHO-057	CHO-058 CHO-059		
2.4-diflucrobenzaldehyde	J.o-Dimethyi-Anydroxydenzaide Tryde	3-Critoro-4-nyaroxy-5-t-outyiben zaldehyde	
CHO-060	CHQ-061	CHO-0e5	
		· · · · · · · · · · · · · · · · · · ·	
4-Ethoxy-3-methoxybenzalgehy de	2-Nitrothiophene-4-carboxalden yde	4-(Dibutylamino)berzaldehyde	
CHO-063	CHO-064	CHO-065	
-(Trifluoromethyl)benzaldehyde	4,6-Olmethoxy-salicylaldehyde	2,3,4-Trihydroxyberizaldehyde	
CHO-066	CHO-067 CHO-068		
2-Hydroxy-3-methoxyoenzaideh]	(5-Herma 2.4 d.5-de-		
yde	5-Bromo-3,4-dinydroxybenzalde hyde	3,4-Diacetoxybenzaldehyde	
CHO-069	CHO-070	CHO-071	

Table 12 (continued)

	2-Bromobenzaldehyde	2.4-Cihydroxycenzaldenyde
CHO-072	CHO-073	CHO-374
z-nygroxy-4-methoxypenzalgen yde	3-Bromobenzaidehyde	3.5-Ui-lert-curyi-2-nydroxyoeriza Idenyde
CHO-075	CHO-376	CH C- 377
4-Carboxybenzaidehyde	4-Dimethylamino-T-napmnaiden yde	4-Hydraxy-3-ratropenzaldenyde
CHO-078	CHO-079	CHO-080
2-Hydroxy-4-metrioxydenzaiden yde	3-Hydroxy-4-nitrobertzalcehyde	4-Bromopenzaldehyde
CHO-081	CHO-082	CHO-083
· · · · · · · · · · · · · · · · · · ·		
2,3,5,7-Tetrahydro-ð-hydroxy-1 H,5H-benzo(ij]quinolizina.9 carboxaldehyde	3.5-Diisopropyl-Litydroxybenzal dehyde	Benzo(b)furan-2-carboxaldenyde
H,5H-benzo(ij)quinalizine.9		Benzo(b]furan-2-carboxaldenyde CHO-086
H,5H-benzo(ij]quinolizina.9 carboxaldehyde CHO-084	denyde	
H,5H-benzo(ij]quinolizina.9 carboxaldehyde CHO-084	CHO-085	
H,5H-benzo(j)quinolizina.9 carboxaldehyde CHO-084 3.5-Cllodo-4-methyl-2-pyrrolecan boxaldehyde	CHO-085 1-(4-chiorophenyl)pyrrole-2-caroloxaldehyde	CHO-086 5-Elhyl-2-furaldehyde
H.5H-benzo(ij]quinolizina.9 carboxaldehyde CHO-084 1.5-Dliodo-4-methyl-2-pyrrolecar coxaldehyde CHO-087	CHO-085 1-(4-chiorophenyl)pyrrole-2-caro axaldehyde CHO-088	CHO-086 5-Ethyl-2-furaldehyde CHO-089 6-Bromo-2-hydroxy-3-methoxyd
H,5H-benzo(ij]quinolizina.9 carboxaldehyde CHO-084 3.5-Cliodo-4-methyl-2-pyrrolecar boxaldehyde CHO-087 3.4-Oimethyithiano(b]dhiopnene- 2-carboxaldehyde	CHO-085 1-(4-chiorophenyl)pyrrole-2-carolaxaldehyde CHO-088 3-Bromouriophene-2-carooxaldelhyde	CHO-086 5-Ethyl-2-furaldehyde CHO-089 6-Bromo-2-hydroxy-3-methoxyo enzaldehyde

Table 12 (continued)

6-Methoxy-4-methylsailcylaiden yde	Ethyl 2,4-Dimethyl-5-formy-3-pyrrolec arboxylare	4-stryk-o-icrmy-J-methyk-2-pyrrol lecarboxylic add
CHC-096	СНО-098	
Emyi-3-iormy-1,2,4-mmethyl-3-o ymolecarboxylate	4-(4-romyipiperazine-1-yi)beriz sidehyde	4-(4-romyimorphonino-1-yi)ben zaldenyde
CHO-033	CHO-100	CHO-101
5-Chioro-3-memoxycaroonyi-4-methoxycarbonyimethyl-pyrrole- 2-carboxaldehyde	1-(4-cnioroperzyi)crcmo-pyra zole-5-carboxaldehydə	lmicazole 4-caroxxaldettyde
CHC-102	CHO-163	CHO-104
4-Chioro-pyrazoie-5-cardoxalde hyde	b-einoxycaroonyi 4-methyi-J-me thylcarbonyi-pymcle-2-carboxaid enyde	5-1-Buryi-4-nyaroxy-3-logoperizati denyde
CHO-105	CHO-106	CHO-107
5-Bromofuran-2-carboxaldehyde	1,4-Dimethyl-3-formylcarbazole	1.4-Oinydroxy-2-rormyk-3.5.7.3-3 etratnydronaphthalene
CHO-108	CHO-109	CHO-110
5-fluoroisatin	3,4-dimethyl-2-formylpyrrole	isatin
CHÖ-111	CHO-112	CHO-113
5-ethyl-2-formylthiophene	4-methoxybenzaldehyde	4-diethylaminobenzaldehyde
CHO-114	CHO-115 CHO-116	
3,5-diethylpyrrole-2-carboxaldeh yde	5-Benzyloxylindole-3-carboxalde hyde	3-Bromo-5-cnloro-2-hydroxyben zaldehyde
CHO-117	CHO-118	CHO-119

Table 12 (continued)

(4-cniorapnenyithio)cenzaioen	6-Спотерірегспаі	Chromone-3-carboxaldehyde	
CHO-120	CHO-121	CHO-122	
3-Cyanobenzaldenyde	4-Cyanobenzalcehyde	o.d-Dichicroctromone-J-carbox aldehyde	
CHO-123	CHO-124 CHO-125		
2.5-cihycroxybenzaidenyde	2,3-Dimethoxybertzaldehyde 2,4-Dimethoxybert		
CHO-126	CHO-127	CHO-123	
2,5-Cimethoxybercaldehyde	2.5-Oimethoxybenzaldehyde,	3,5-Oimethoxyperzzicenyde	
CHO-129	CHQ-130	CHO-131	
	<u> </u>	<u> </u>	
-Dimethylamino-2-methoxypen laidehyde	3,4-Dimethylbenzaldehyde	5,7-Dimethylchromone-3-carco aldehyde	
	3,4-Dimethylbenzaklahyde CHO-133		
aldehyde		aldehyde	
CHO-132	CHO-133	aldehyde CHO-134	
CHO-132 S-Ethylfurfural	CHO-133 Ferrocenecarboxaldehyde	CHO-134 Flucrene-2-carboxaldertyde	
S-Ethylfurfural CHO-135 2-Fiuoro-3-(Iniluoromethyl)cenz	CHO-133 Ferrocenecarboxaldehyde CHO-138 2-Fluoro-4-(bifluoromethyl)benz	CHO-134 Flucrone-2-carboxalderryde CHO-137	
CHO-132 S-Ethylfurfural CHO-135 2-Fiuoro-3-(tniiuoromethyl)penz	CHO-133 Ferrocenecarboxaldehyde CHO-138 2-Fluorc-4-(trilluoromethyr)benz aldehyde	CHO-134 Flucrene-2-carboxaldenyde CHO-137 2-Huoro-5-(Influoromethyl)der aldehyde	

Table 12 (continued)

2-Methoxy-1-naphthaldehyde	4-Methoxy-1-naphthaldehyde	4-(Methyithio)berzaldehyde
CHC-144	CHO-145	CHO-146
[3-Methyithiocnene-2-carpoxalde]	5-Vernyithioprene-Z-carcoxaide	
hyde	hyde	pentamethylbenzaldehyde
CHO-147	CHO-148	CHO-149
3-Phenoxybenzaidehyce	Pyridine-2-carboxaidehyde	Pyridine-3-carboxaldehyde
CHO-150	CHO-151	CHO-152
Pyndlne-4-carcoxaldshyde	4-Pyrrclidincoerazidenyoe. 98+%	1,2,3,6-Tetrahydropenzaldehyde
CHQ-153	CHO-154	CHO-155
2,3,4-Trimethoxyberizaklehyde	2,4,5-Trimethoxybenzaldehyde	2,4,6-Trimethaxytenzaldenyde
2,5,4-1 mined oxyodical denyde	2,4,3-11lifetioxyddiaeadeilyde	2,4,64 milled dayoen aade lyde
CHO-158	CHO-157	CHO-158
	1-Acetyi-3-indolecarboxaidenyd	
3,4,5-Trimethoxyberizaldehyde	e	6-Chloro-3-formylchromone
CHO-159	CHO-160	CHO-161
[6-Chloro-3-formyl-7-memylchra]		2-Chioro-3-quinolinecarboxalgeri
mone	5-(2-Chloropherryl)furfural	yde
CHO-162	CHO-163	CHO-164
6,8-Dibramo-3-formylchromane	2,5-Dimethoxy-3-letrahydrofurac arboxaldehyde	4,5-Oimethyl-2-furaldehyde
	S. S. Carlottiy Co.	
CHO-165	CHO-166	CHO-167
		· · · · · · · · · · · · · · · · · · ·

Table 12 (continued)

2-Formyi-6,7-cimetryichromone	3-formyl-6, 8-almethylchromone	
CHO-169	СНО-170	
3-formyl-6-methylchromone	3-formy+6-naroctromone	
CHO-172 CHO-173		
z-Methcxylndole-J-carboxalden yde	1-Methyűsatin	
CHO-175	CHO-176	
(S)-(-)-Perillaldenyde	2-(Trifluoroacetyi)thiopinene	
CHO-178	CHO-179	
4-oenzyioxy-3,5-diisopropyibenz aldehyde CHO-181	3-(-outy)-4-methoxyteenzaldenyd e CHO-182	
3-bromo-5-l-butyl-4-methoxycen zaldetryde	4-benzyloxy-3-bromo-5-l-butylbe nzaldenyde	
CHO-184	CHO-185	
A-cenzyloxy-3-2-butyl-5-chlorobel rozaldehyde	34-outyl-54000-4-methoxyberiza Idehyde	
CHO-187	CHO-188	
3-1-butyl-4-methoxy-5-nitrooenza Idenyde	4-benzyloxy-3-2-buryl-5-nurober zaldehyde	
CHO-190 CHO-191		
	CHO-169 3-formyl-6-methylchromone CHO-172 E-Methoxylndole-3-carboxalden yde CHO-175 (S)-(-)-Perillaldenyde CHO-178 4-oenzyloxy-3,5-dilsopropylbenz aldehyde CHO-181 3-bromo-5-4-butyl-4-methoxyben zaldehyde CHO-184 4-oenzyloxy-3-1-butyl-5-chlorobe rzaldehyde CHO-187	

Table 12 (continued)

3,3-ai-t-auryi-4-methaxyoenzala ehyde	denyde	1.5-aimethyi-4-me:naxybenzaia enyde
CHO-192	CHO-193	CHO-194
Loenzyloxy-3,5-almethylbenzal denyde	5-oromo-2-nydroxy-3-methoxy-olenzaldehyde	S-bromosalicyaldenyce 201
CHO-195	CHO-196	CHO-197
2-nyarcxy-5-nitrocenzaldehyde	+nyaroxy-2-nira-3-methoxyoe nzaldehyde	3-acroxysalicyaldenyde
CHO-198	CHC-199	CHO-200
3,5-alchiarosalicylaidehyde	5-chlorosalicyaldehyde	4-(dlethylamino)salicyaidehyde*
CHO-201	CHO-202	CHO-203
5-(Influorome:hoxy)salicylaideny de	3,5-dibromosalicyaldehyde	3-fluoresalicyaldehyde
CHO-204	CHO-205	CHQ-206
3-brcmo-4-nydroxybenzaidenyd e	5-chiorosalicyaldehydə	2-4,dimethyl-5-formylpyrrole
CHO-207	207 CHO-208 CHO-209	
3,5-diisopropyl-2-formylpyrrole	3,5-dimethyithlophene-2-carbox aldehyde	3-methyl-5-ethylthiophene-2-car boxaldehyde
CHO-210	CHO-211 CHO-212	
3-methyl-5-isopropylthlophene-2 -carboxaldehyde	3-methyl-5-cyclopentylmethylthi ophene-2-carboxaldehyde	3-methyl-5-cyclopropytthiophene -2-carboxaldehyde
CHO-213	CHO-214	CHO-215

CHO-237

Table 12 (continued)

-methyl-5-2thylthlopnene-2-car boxaldenyde	4-methyl-5-scoropythiopnene-2 -carboxaldehyde	4-metnyl-3-cyclopentylmethyithli ophene-2-carboxaldenyde
CHC-218	CHO-217	CHO-218
4-methyl-5-cyclopropylmethylthl cohene-2-carboxaldehyde	5-isopropyithiophene-2-carboxal dehyde	5-onenyimethyithiophene-2-cart oxaldehyde
CHC-Z19	. СНО-220	CHO-221
5-cyclchexylmethylthloohene-2- carboxaldehyde	5-c/dohexyithiophene-2-carbox aldehyde	5-phenyithlophene-2-carboxald
CHC-222	CHO-223 CHO-224	
3-methyl-5-oropylthicphene-2-ca boxaldehyde	3-methyl-5-cyclohexylmethylthio phene-2-carboxaldehyde	4-methyl-5-propylthiophene-2-c rboxaldehyde
CHO-225	CHO-226	CHO-227
	5-n-butytthiophene-2-carboxalde hyde	5-cyclopropylmethylthiophene- carboxaldenyde
phene-2-carboxaldehyde	hyde	CHO-230
phene-2-carboxaldehyde CHO-228 5-cyclopropylthiophene-2-carbo	CHO-229 3-methyl-5-phenylmethylthiophe	CHO-230 CHO-230 4-methyl-5-phenylmethylthioph
5-cyclopropylthiophene-2-carbo xaldehyde	CHO-229 3-methyl-5-phenylmethylthiophene-2-carboxaldehyda	CHO-230 4-methyl-5-phenylmethylthioph ne-2-carboxaldehyde

MASTER	PLATE	PLATE	NAME
BARCODE	ROW	COLUMN	NAME
		=====================================	1
10717	A	2	3-(2-ethoxybenzylidenyl)-5.7-dibromo-2-indolinone
			, , , , , , , , , , , , , , , , , , ,
10717	A	3	3-[(thien-2-yl)methylidenyl]-5.7-dibromo-2-
			indolinone
ļ	i		
10717	A	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5,7-dibromo-2-
			indolinone
40747			
10717	A	5	3-(4-fluorobenzylidenyl)-5,7-dibromo-2-indolinone
10717			
10/1/	Α	6	3-[(indol-3-yl)methylidenyl]-5,7-dibromo-2- indolinone
			indoithone
10717	- A	7	3-[(2-methylthien-5-yt)methylidenyl]-5,7-dibromo-2-
		•	indolinone
10717	A	8	3-(4-bromobenzylidenyl)-5,7-dibromo-2-indolinone
		-	- (
	ļ		
10717	A	9	3-[(pyrrol-2-yl)methylidenyl]-5,7-dibromo-2-
		-	indolinone
10717	Α	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5,7-dibromo-
İ			2-indolinone
10717	Α	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-
İ	-		5,7-dibromo-2-ındolinone
10717	В	2	3-(2-ethoxybenzylidenyl)-5-iodo-2-indolinone
	ĺ	ļ	
10717	В	3	2 (/high 2 ::)\
10717	В	3	3-[(thien-2-yl)methylidenyl]-5-iodo-2-indolinone
1	1	describe	
10717	В	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5-iodo-2-
		7	indolinone
	1	ļ	asions
10717	В	5	3-(4-fluorobenzylidenyl)-5-iodo-2-indolinone
1			, and a substitution of the substitution of th
10717	В	6	3-[(indol-3-yl)methylidenyl]-5-iodo-2-indolinone
		ļ	. , , , , , , , , , , , , , , , , , , ,
	_	ĺ	
		<u>-</u>	

40747			
10717	В	7	3-[(2-methylthien-5-yl)methylidenyl]-5-iodo-2- indolinone
10717	- В	8	3-(4-bromobenzylidenyl)-5-iodo-2-indolinone
10717	В	9	3-[(pyrrol-2-yl)methylidenyl]-5-iodo-2-indolinone
10717	В	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5-iodo-2- indolinone
10717	В	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone
10717	С	2	3-(2-ethoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10717	С	3	3-{(thien-2-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10717	С	4	3-[(1-methylpyrrol-2-yl)methylidenyi]-5-bromo-4- methyl-2-indolinone
10717	С	5	3-(4-fluorobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10717	С	6	3-[(indol-3-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10717	С	7	3-[(2-methylthien-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10717	С	8	3-(4-bromobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10717	С	9	3-[(pyrrol-2-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10717	С	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10717	С	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10717	D	2	3-(2-ethoxybenzylidenyl)-5-methylaminosulfonyl-2- indolinone
	L		_ -

120 Table 13 (continued)

10717		·	
10717	D	3	3-[(thien-2-yl)methylidenyl]-5-methylaminosuifonyl- 2-indolinone
10717	- D	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10717	D	5	3-(4-fluorobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
10717	D	6	3-[(indol-3-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone
10717	D	7	3-[(2-methylthien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10717	D	8	3-(4-bromobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
10717	D	9	3-[(pyrrol-2-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone
10717	D	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10717	D	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10717	E	2	3-(2-ethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	3	3-[(thien-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	5	3-(4-fluorobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	6	3-[(indol-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	7	3-[(2-methylthien-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10717	E	8	3-(4-bromobenzylidenyl)-5-[4- (triffuoromethyl)phenylaminosulfonyl]-2-indolinone

121 Table 13 (continued)

E	9	3-[(pyrroi-2-yi)methylidenyi]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5-;4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
F	2	3-(2-ethoxybenzylidenyl)-5-(morpholin-1-yl)sulfonyl- 2-indolinone
F	3	3-[(thien-2-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5-(morpholin- 1-yl)sulfonyl-2-indolinone
F	5	3-(4-fluorobenzylidenyl)-5-(morpholin-1-yl)sulfonyl- 2-indolinone
F	6	3-[(indol-3-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	7	3-[(2-methylthien-5-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	8	3-(4-bromobenzylidenyl)-5-(morpholin-1-yl)sulfonyl- 2-indolinone
F	9	3-[(pyrrol-2-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5-(morpholin- 1-yl)sulfonyl-2-indolinone
F	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
G	2	3-(2-ethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
G	3	3-{(thien-2-yl)methylidenyl}-5-(2-chloroethyl)-2- indolinone
G	4	3-[(1-methylpyrrol-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
	F F F G G	E 10 E 11 F 2 F 3 F 6 F 7 F 8 F 9 F 10 F 11 G 2 G 3

122 Table 13 (continued)

10717			
	G	5	3-(4-fluorobenzylidenyi)-5-(2-chloroethyi)-2- indolinone
10717	G	6	3-[(indol-3-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone
10717	G	7	3-[(2-methylthien-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10717	G	8	3-(4-bromobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10717	G	9	3-[(pyrrol-2-yi)methylidenyi]-5-(2-chloroethyl)-2- indolinone
10717	G	10	3-(2-hydroxy-6-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10717	G	11	3-[(3,4-dibromo-2-methylpyrrol-5-yl)methylidenyl]-5- (2-chloroethyl)-2-indolinone
10718	A	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone
10718	A	3	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10718	A	4	3-{(1-hydroxynapth-2-yl)methylidenyl}-5,7-dibromo- 2-indolinone
10718	A	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- (ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]- 5,7-dibromo-2-indolinone
10718	A	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5,7-dibromo-2-indolinone
10718	A	7	3-[(2,3-dimethoxycarbonyl-5-methylpyrrol-4- yl)methylidenyl]-5,7-dibromo-2-indolinone
10718	А	8	3-(4-chloro-3-nitrobenzylidenyl)-5,7-dibromo-2- indolinone
10718	A	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5,7- dibromo-2-indolinone
10718	A	10	3-[(furan-2-yl)methylidenyl]-5,7-dibromo-2- indolinone

123
Table 13
(continued)

A	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5,7-dibromo-2- indolinone
- B	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5- yl)methylidenyl]-5-iodo-2-indolinone
8	3	3-(3-bromo-2-hydroxy-5-methoxybenzytidenyl)-5- iodo-2-indolinone
В	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5-iodo-2- indolinone
В	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- (ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- iodo-2-indolinone
В	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-iodo-2-indolinone
В	7	3-[(2,3-dimethoxycarbonyl-5-methylpyrrol-4- yl)methylidenyl]-5-iodo-2-indolinone
В	8	3-(4-chloro-3-nitrobenzylidenyl)-5-iodo-2-indolinone
В	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5-iodo-2- indolinone
В	- 10	3-[(furan-2-yl)methylidenyl]-5-iodo-2-indolinone
В	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5-iodo-2- indolinone
С	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5- yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
С	3	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
С	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
С	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- (ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- bromo-4-methyl-2-indolinone
С	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
	B B B B C C C C	B 2 B 3 B 4 B 5 B 6 B 7 B 8 C 2 C 3 C 4 C 5

40740	1		
10718	С	7	3-[(2,3-dimethoxycarbonyl-5-methylpyrrol-4-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
10718	- C	8	3-(4-chloro-3-nitrobenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10718	C ·	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5-bromo-4- methyl-2-indolinone
10718	С	10	3-[(furan-2-yi)methylidenyi]-5-bromo-4-methyl-2- indolinone
10718	С	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10718	D	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5- yl)methylidenyl]-5-methylaminosulfonyl-2- indolinone
10718	D	3	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10718	D	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10718	D	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- (ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone
10718	D	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-methylaminosulfonyl-2- indolinone
10718	D	7	3-{(2,3-dimethoxycarbonyl-5-methylpyrrol-4- yl)methylidenyl]-5-methylaminosulfonyl-2- indolinone
10718	D	8	3-(4-chloro-3-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10718	D	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10718	D	10	3-[(furan-2-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone
10718	D	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10718	E	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5- yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone

E	3	
	J	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	5	3-[(2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- ethoxycarbonylmethyl-pyrrol-5-yl)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2-
E	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	7	3-[(2,3-dimethoxycarbonyl-5-methylpyrrol-4- yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	8	3-(4-chloro-3-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	9	3-(2.4-dihydroxy-3-methylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	10	3-[(furan-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
F	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5- yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
F	3	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5-(morpholin- 1-yl)sulfonyl-2-indolinone
F	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl-4- (ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
F	7	3-[(2,3-dimethoxycarbonyl-5-methyl-pyrrol-4- yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
F	8	3-(4-chloro-3-nitrobenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
		E 5 E 6 E 7 E 8 E 9 E 10 E 11 F 2 F 3 F 6 F 7

126
Table 13
(continued)

10710			
10718	F	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10718	F	10	3-[(furan-2-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10718	F	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10718	G	2	3-[(2,4-dimethyl-3-ethoxycarbonylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10718	G	3	3-(3-bromo-2-hydroxy-5-methoxybenzylidenyl)-5- (2-chloroethyl)-2-indolinone
10718	G	4	3-[(1-hydroxynapth-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10718	G	5	3-[[2-ethoxycarbonyl-3-(2-ethoxycarbonyl)ethyl- 4(ethoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- (2-chloroethyl)-2-indolinone
10718	G	6	3-[(2-methyl-3-ethoxycarbonylfuran-5- yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10718	G	7	3-{(2,3-dimethoxycarbonyl-5-methylpyrrol-4- yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10718	G	. 8	3-(4-chloro-3-nitrobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10718	G	9	3-(2,4-dihydroxy-3-methylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10718	G	10	3-[(furan-2-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone
10718	G	11	3-[(2-nitrofuran-5-yl)methylidenyl]-5-(2-chloroethyl)- 2-indolinone
10719	A	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5,7-dibromo-2-indolinone
10719	A	3	3-(3,4-dihydoxybenzylidenyl)-5,7-dibromo-2- indolinone
10719	A	4	3-(2,4-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone

127 Table 13 (continued)

10719	A	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]- 5,7-dibromo-2-indolinone
10719	- A	6	3-(2,4,6-trimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10719	A	7	3-(4-hydroxybenzylidenyl)-5,7-dibromo-2-indolinone
10719	A	8	3-(4-dimethylaminobenzylidenyl)-5,7-dibromo-2- indolinone
10719	A	9	3-(2-chloro-4-fluorobenzylidenyl)-5,7-dibromo-2- indolinone
10719	A	10	3-(3-nitrobenzylidenyl)-5,7-dibromo-2-indolinone
10719	A	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5,7- dibromo-2-indolinone
10719	В	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5-iodo-2- indolinone
10719	В	3	3-(3,4-dihydoxybenzylidenyl)-5-iodo-2-indolinone
10719	В	- 4	3-(2,4-dimethoxybenzylidenyı)-5-iodo-2-ındolınone
10719	В	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- iodo-2-indolinone
10719	В	6	3-(2,4,6-trimethoxybenzylidenyl)-5-iodo-2- indolinone
10719	В	7	3-(4-hydroxybenzylidenyl)-5-iodo-2-indolinone
10719	В	8	3-(4-dimethylaminobenzylidenyl)-5-iodo-2- indolinone
10719	В	9	3-(2-chloro-4-fluorobenzylidenyl)-5-iodo-2- indolinone
10719	8	10	3-(3-nitrobenzylidenyl)-5-iodo-2-indolinone

Table 13 (continued)

10719	В	11	: 3-[4-fluoro-2-(trifluoromethyl)benzyl:denyl]-5-iodo-2- indolinone
10719	- C	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10719	С	3	3-(3,4-aihydoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10719	С	4	3-(2,4-dimethoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10719	С	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10719	С	6	3-(2,4,6-trimethoxybenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10719	С	7	3-(4-hydroxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10719	С	8	3-(4-dimethylaminobenzylidenyl)-5-bromo-4- methyl-2-indolinone
10719	С	9	3-(2-chloro-4-fluorobenzylidenyl)-5-bromo-4- methyl-2-indolinone
10719	С	10	3-(3-nitrobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10719	С	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5-bromo- 4-methyl-2-indolinone
10719	D	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10719	D	3	3-(3,4-dihydoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10719	D	4	3-(2,4-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10719	D	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10719	D	6	3-(2,4,6-trimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone

129
Table 13
(continued)

10719	D	7	3-(4-hydroxybenzylidenyl)-5-methylaminosulfonyl- 2-indolinone
10719	- D	8	3-(4-dimethylaminobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10719	D	9	3-(2-chloro-4-fluorobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10719	D	10	3-(3-nitrobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
10719	D	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10719	E	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	3	3-(3,4-dihydoxybenzytidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	4	3-(2,4-dimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
10719	E	6	3-(2,4,6-trimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	7	3-(4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	8	3-(4-dimethylaminobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	9	3-(2-chloro-4-fluorobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	10	3-(3-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	E	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10719	F	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5-(morpholin- 1-yl)sulfonyl-2-indolinone

130 Table 13 (continued)

10719	F	3	3-(3,4-dihydoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	- F	4	3-(2,4-dimethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	F	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10719	F	6	3-(2,4,6-trimethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	F	7	3-(4-hydroxybenzyfidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	F	8	3-(4-dimethylaminobenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	F	9	3-(2-chloro-4-fluorobenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10719	F	10	3-(3-nitrobenzylidenyl)-5-(morpholin-1-yl)sulfonyl-2- indolinone
10719	F	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10719	G .	2	3-(4-ethoxy-3-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10719	G	3	3-(3,4-dihydoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10719	G	4	3-(2,4-dimethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10719	G	5	3-[(2,4-dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5- (2-chloroethyl)-2-indolinone
10719	G	6	3-(2,4,6-trimethoxybenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
10719	G	7	3-(4-hydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10719	G	8	3-(4-dimethylaminobenzylidenyl)-5-(2-chloroethyl)- 2-indolinone

131 Table 13 (continued)

10719	G	9	3-(2-chloro-4-fluorobenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
10719	- G	10	3-(3-nitrobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10719	G	11	3-[4-fluoro-2-(trifluoromethyl)benzylidenyl]-5-(2- chloroethyl)-2-indolinone
10720	A	2	3-(2,4,6-trifluorobenzylidenyl)-5,7-dibromo-2- indolinone
10720	A	3	3-(4-nydroxy-2-methoxybenzylidenyl)-5,7-dibromo- 2-indolinone
10720	A	4	3-(3,4-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10720	A	5	3-(2-hydroxybenzylidenyi)-5,7-dibromo-2-indolinone
10720	A	6	3-benzylidenyl-5,7-dibromo-2-indolinone
10720	A	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5,7- dibromo-2-indolinene
10720	A	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5,7- dibromo-2-indolinone
10720	A	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10720	A	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5,7-dibromo- 2-indolinone
10720	A	11	3-[(imidazol-2-yi)methylidenyi]-5,7-dibromo-2- indolinone
10720	В	2	3-(2,4,6-trifluorobenzylidenyl)-5-iodo-2-indolinone
10720	В	3	3-(4-hydroxy-2-methoxybenzylidenyl)-5-iodo-2- indolinone
10720	В	4	3-(3,4-dimethoxybenzylidenyl)-5-iodo-2-indolinone

132
Table 13
(continued)

10720	В	5	3-(2-hydroxybenzylidenyl)-5-iodo-2-indolinone
10720	В	6	3-benzylidenyl-5-iodo-2-indolinone
10720	В	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5- iodo-2-indolinone
10720	В	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5-iodo-2- indolinone
10720	В	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5-iodo-2- indolinone
10720	В	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5-iodo-2- indolinone
10720	В	11	3-[(imidazol-2-yl)methylidenyl]-5-iodo-2-indolinone
10720	С	2	3-(2,4,6-trifluorobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10720	С	3	3-(4-hydroxy-2-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10720	С	4	3-(3,4-dimethoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10720	С	5	3-(2-hydroxybenzylidenyl)-5-bromo-4-methyl-2- indolinane
10720	С	6	3-benzylidenyl-5-bromo-4-methyl-2-indolinone
10720	С	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10720	С	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5-bromo-4- methyl-2-indolinone
10720	С	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10720	С	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
	·		_ <u>- </u>

133
Table 13
(continued)

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10720	C	11	3-[(Imidazol-2-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10720	D	2	3-(2,4,6-trifluorobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10720	D	3	3-(4-hydroxy-2-methoxybenzylidenyi)-5- methylaminosulfonyl-2-indolinone
10720	D	4	3-(3,4-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10720	D	5	3-(2-hydroxybenzylidenyl)-5-methylaminosulfonyl-2- indolinone
10720	D	6	3-benzylidenyl-5-methylaminosulfonyl-2-indolinone
10720	D	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10720	D	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10720	D	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10720	D	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10720	D	11	3-[(imidazol-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10720	E	2	3-(2,4,6-trifluorobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	3	3-(4-hydroxy-2-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	4	3-(3,4-dimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	5	3-(2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	6	3-benzylidenyl-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone

134
Table 13
(continued)

10720	E	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5-[4-
	_	·	(trifluoromethyl)phenylaminosulfonyl]-2-indolinane
10720	E	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	Ε	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	E	11	3-[(imidazol-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10720	F	2	3-(2,4,6-trifluorobenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10720	F	3	3-(4-hydroxy-2-methoxybenzylidenyl)-5-(morpholin- 1-yl)sulfonyl-2-indolinone
10720	F	4	3-(3,4-dimethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10720	F	5	3-(2-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10720	F	6	3-benzylidenyl-5-(morpholin-1-yl)sulfonyl-2- indolinone
10720	F	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10720	F	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10720	F	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10720	F	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5-(morpholin- 1-yl)sulfonyl-2-indolinone
10720	F	11	3-[(imidazol-2-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10720	G	2	3-(2,4,6-trifluorobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
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135
Table 13
(continued)

G	3	3-(4-hydroxy-2-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
G	4	3-(3,4-dimethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
G	5	3-(2-hydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
G	6	3-benzylidenyl-5-(2-chloroetnyl)-2-indolinone
G	7	3-[(2-methylmercaptothien-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
G	8	3-(2,4-dihydroxy-6-methylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
G	9	3-(3-ethoxy-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
G	10	3-(2-hydroxy-5-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
G	11	3-[(imidazol-2-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone
A .	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5,7- dibromo-2-indolinone
A	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5,7- dibromo-2-indolinone
A	4	3-[(2,3-dimethylthien-5-yl)methylidenyl]-5,7- dibromo-2-indolinone
À	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5,7- dibromo-2-indolinone
Α	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)- 5,7-dibromo-2-indolinone
A	7	3-[(2-chlorothien-5-yl)methylidenyl]-5,7-dibromo-2- indolinone
Α	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5,7- dibromo-2-indolinone
	G G G A A A A	G 4 G 5 G 6 G 7 G 8 G 9 G 10 G 11 A 2 A 3 A 4 A 5 A 6 A 7

136 Table 13 (continued)

10721	A	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10721	A	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10721	A	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10721	В	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5-iodo- 2-indolinone
10721	В	3	3-[(4-chioro-1-methylpyrazol-3-yl)methylidenyl]-5- iodo-2-indolinone
10721	В	4	3-[(2,3-dimethylthien-5-yl)methylidenyl]-5-iodo-2- indolinone
10721	В	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5-iodo- 2-indolinone
10721	В	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)-5- iodo-2-indolinone
10721	В	7	3-[(2-chlorothien-5-yl)methylidenyl]-5-iodo-2- indolinone
10721	В	8	3-{(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-iodo-2- indolinone
10721	В	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5-iodo-2- indolinone
10721	В	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5-iodo- 2-indolinone
10721	В	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5-iodo-2- indolinone
10721	С	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10721	С	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10721	С	4	3-[(2,3-dimethylthien-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
 			<u> </u>

Table 13 (continued)

10721	С	5	3-{(4,5,6,7-tetrahydroindol-2-yl)methylidenyi}-5- bromo-4-methyl-2-indolinone
10721	С	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)-5- bromo-4-methyl-2-indolinone
10721	С	7	3-[(2-chlorothien-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10721	С	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10721	С	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10721	С	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10721	С	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10721	D	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	Ō	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	D		3-[(2,3-dimethylthien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	D	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	D	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzyliaenyl]-5- methylaminosulfonyl-2-indolinone
10721	D	7	3-[(2-chlorothien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	D	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10721	O	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10721	D	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone

10721	D	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5-
10/21	U	''	methylaminosulfonyl-2-indolinone
10721	E	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	4	3-[(2,3-dimethylthien-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
10721	E	7	3-[(2-chlorothien-5-yl)methylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	E	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10721	F	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	4	3-[(2,3-dimethylthien-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)-5- (morpholin-1-yl)sulfonyl]-2-indolinone
<u>-</u>			<u> </u>

Table 13 (continued)

10721	F	7	3-[(2-chlorothien-5-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl]-2-indolinone
10721 -	F	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl]-2-indolinone
10721	F	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	F	11	3-(3,5-d)-t-butyl-4-hydroxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl]-2-indolinone
10721	G	2	3-[(1-methylbenzimidazol-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	3	3-[(4-chloro-1-methylpyrazol-3-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	4	3-{(2,3-dimethylthien-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	5	3-[(4,5,6,7-tetrahydroindol-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	6	3-(3-chloromethyl-2-hydroxy-5-nitrobenzylidenyl)-5- (2-chloroethyl)-2-indolinone
10721	G	7	3-[(2-chlorothien-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	8	3-[(2,4-dimethylpyrrol-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10721	G	9	3-(3-t-butyl-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10721	G	10	3-(3-bromo-5-t-butyl-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10721	G	11	3-(3,5-di-t-butyl-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10722	A	2	3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5,7- dibromo-2-indolinone
\		 	

140 Table 13 (continued)

10722				
10722	10722	A	3	3-(2,4,6-trihydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10722	10722	A	4	
10722	10722	A	5	3-(4-carooxybenzylidenyl)-5,7-dibromo-2-indolinone
10722 A 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5,7-dibromo-2-indolinone	10722	A	6	
10722	10722	A	7	
10722	10722	A	8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10722 A	10722	A	9	
10722 B 2 3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5-iodo-2-indolinone 10722 B 3 3-(2,4,6-trihydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 4 3-{(2-nitrothien-5-yl)methylidenyl}-5-iodo-2-indolinone 10722 B 5 3-(4-carboxybenzylidenyl)-5-iodo-2-indolinone 10722 B 6 3-(2,4-difluorobenzylidenyl)-5-iodo-2-indolinone 10722 B 7 3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722	10722	A	10	
10722 B 3 3-(2,4,6-trihydroxybenzylidenyl)-5-iodo-2-indolinone	10722	A	11	
10722 B 4 3-{(2-nitrothien-5-yl)methylidenyl}-5-iodo-2-indolinone 10722 B 5 3-(4-carboxybenzylidenyl)-5-iodo-2-indolinone 10722 B 6 3-(2,4-difluoropenzylidenyl)-5-iodo-2-indolinone 10722 B 7 3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-	10722	В		
10722 B 5 3-(4-carboxybenzylidenyl)-5-iodo-2-indolinone	10722	В	3	3-(2,4,6-trihydroxybenzylidenyl)-5-iodo-2-indolinone
10722 B 6 3-(2,4-difluorobenzylidenyl)-5-iodo-2-indolinone 10722 B 7 3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-	10722	В	4	
10722 B 7 3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-	10722	В	5	3-(4-carboxybenzylidenyl)-5-iodo-2-indoiinone
indolinone 10722 B 8 3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-iodo-	10722	В	6	3-(2,4-difluorobenzylidenyl)-5-iodo-2-indolinone
[[[]]]]] [[] [] [] [] [] [10722	В	7	
	10722	В	8	

141 Table 13 (continued)

40700			
10722	В	9	3-[(2-nitrothien-4-yi)methylidenyl]-5-iodo-2- indolinone
10722	В	10	3-(4-di-n-butylaminobenzylidenyl)-5-iodo-2- indolinone
10722	В	11	3-[4-(trifluoromethyl)benzylidenyl]-5-iodo-2- indolinone
10722	С	2	3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5- dibromo-4-methyl-2-indolinone
10722	С	3	3-(2,4,6-trihydroxybenzylidenyl)-5-dibromo-4- methyl-2-indolinone
10722	С	4	3-[(2-nitrothien-5-yl)methylidenyl]-5-dibromo-4- methyl-2-indolinone
10722	С	5	3-(4-carboxybenzylidenyl)-5-dibromo-4-methyl-2- indolinone
10722	С	6	3-(2,4-difluorobenzylidenyl)-5-dibromo-4-methyl-2- indolinone
10722	С	7	3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-dibromo- 4-methyl-2-indolinone
10722	С	. 8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5- dibromo-4-methyl-2-indolinone
10722	C	9	3-[(2-nitrothien-4-yl)methylidenyl]-5-dibromo-4- methyl-2-indolinone
10722	С	10	3-(4-di-n-butylaminobenzylidenyl)-5-dibromo-4- methyl-2-indolinone
10722	С	11	3-[4-(trifluoromethyl)benzylidenyl]-5-dibromo-4- methyl-2-indolinone
10722	D	2	3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10722	О	3	3-(2,4,6-trihydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10722	D	4	3-[(2-nitrothien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone

40700			
10722	D	5	3-(4-carboxybenzylidenyi)-5-methylaminosuifonyl-2- indolinone
10722	D	6	3-(2,4-difluorobenzylidenyl)-5-methylaminosulfonyl- 2-indolinone
10722	D	7	3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10722	D	8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10722	D	9	3-[(2-nitrothien-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10722	D	10	3-(4-di-n-butylaminobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10722	D	11	3-[4-(trifluoromethyl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10722	Е	2	3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	3	3-(2,4,6-trihydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	-	3-[(2-nitrothien-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	5	3-(4-carboxybenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	6	3-(2,4-difluorobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	7	3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	Ē	8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	9	3-[(2-nitrothien-4-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722	E	10	3-(4-di-n-butylaminobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
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Table 13 (continued)

10722	E	11	3-[4-(trifluoromethyl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10722 -	F	2	3-(3-t-butyl-4-nydroxy-5-nitrobenzylidenyl)-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
10722	F	3	3-(2.4,6-trinydroxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	4	3-[(2-nitrothien-5-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	5	3-(4-carboxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	6	3-(2,4-difluorobenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	7	3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5- (morpholin-1-yl)amınosulfonyl-2-indolinone
10722	F	8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5- (morpholin-1-yl)amınosulfonyl-2-indolinone
10722	F	9	3-[(2-nitrothien-4-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	10	3-(4-di-n-butylaminobenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	F	11	3-{4-(trifluoromethyl)benzylidenyl}-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10722	G	2	3-(3-t-butyl-4-hydroxy-5-nitrobenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10722	G	3	3-(2,4,6-trihydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10722	G	4	3-[(2-nitrothien-5-yl)methylidenyl]-5-(2-chloroethyl)- 2-indolinone
10722	G	5	3-(4-carboxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10722	G	6	3-(2,4-diffuorobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
	.l		

Table 13 (continued)

10722	G	7	3-(3,5-dimethyl-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10722	Ğ	8	3-(3-t-butyl-5-chloro-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10722	G	9	3-[(2-nitrothien-4-yl)methylidenyl]-5-(2-chloroethyl)- 2-indolinone
10722	G	10	3-(4-di-n-butylaminobenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
10722	G	11	3-[4-(trifluoromethyl)benzylidenyl]-5-(2-chloroethyl)- 2-indolinone
10723	A	2	3-(2,3,4-trihydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10723	A	3	3-(2-hydroxy-3-methoxybenzylidenyi)-5,7-dibromo- 2-indolinone
10723	A	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10723	A	5	3-(3,4-diacetoxybenzylidenyl)-5,7-dibromo-2- indolinone
10723	A	6	3-(4-hydroxy-3-methylbenzylidenyl)-5,7-dibromo-2- indolinone
10723	A	7	3-(2-bromobenzylidenyl)-5,7-dibromo-2-indolinone
10723	А	8	3-(2,4-dıhydroxybenzylidenyl)-5,7-dıbromo-2- indolinone
10723	A	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5,7-dibromo- 2-indolinone
10723	A	10	3-(3-bromobenzylidenyl)-5,7-dibromo-2-indolinone
10723	A	11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10723	В	2	3-(2,3,4-trihydroxybenzylidenyl)-5-iodo-2-indolinone
10723	В	2	3-(2,3,4-trihydroxybenzylidenyl)-5-iodo-2-indolinor

145
Table 13
(continued)

10723	В	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5-iodo-2-
10/23			indolinone
10723	В	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5-iodo-2- indolinone
10723	В	5	3-(3,4-diacetoxybenzylidenyl)-5-iodo-2-indolinone
10723	В	6	3-(4-hydroxy-3-methy/benzylidenyl)-5-lodo-2- indolinone
10723	В	7	3-(2-bromobenzylidenyl)-5-iodo-2-indolinone
10723	В	8	3-(2,4-dihydroxybenzylidenyl)-5-iodo-2-indolinone
10723	В	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5-iodo-2- indolinone
10723	В	10	3-(3-bromobenzylidenyl)-5-iodo-2-indolinone
10723	В	11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyl)-5-iodo-2- indolinone
10723	С	2	3-(2,3,4-trihydroxybenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10723	С	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10723	С	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10723	С	5	3-(3,4-diacetoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10723	C	6	3-(4-hydroxy-3-methylbenzylidenyl)-5-bromo-4- methyl-2-indolinone
10723	С	7	3-(2-bromobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10723	С	8	3-(2.4-dihydroxybenzylidenyl)-5-bromo-4-methyl-2- indolinone

146 Table 13 (continued)

С	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
С	10	3-(3-bromobenzylidenyl)-5-bromo-4-methyl-2- indolinone
С	11	3-(3,5-dı-t-butyl-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
D	2	3-(2,3,4-trihydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	5	3-(3,4-diacetoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	6	3-(4-hydroxy-3-methylbenzylidenyi)-5- methylaminosulfonyl-2-indolinone
D	7	3-(2-bromobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
D	8	3-(2,4-dihydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	10	3-(3-bromobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
D	11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
E	2	3-(2,3,4-trihydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
	D D D D D E E	C 10 C 11 D 2 D 3 D 4 D 5 D 6 D 7 D 8 - D 9 D 10 D 11 E 2 E 3

Table 13 (continued)

40700			
10723	E .	5	3-(3,4-diacetoxypenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
			Comments of the second state of the second sta
10723 _	E	6	3-(4-hydroxy-3-methylbenzylidenyl)-5-[4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolmone
10723	E		2 /2
10723		7	3-(2-bromobenzylidenyi)-5-[4- (trifluoromethyl)pnenylaminosulfonyi]-2-indolinone
			, , , , , , , , , , , , , , , , , , , ,
10723	E	8	3-(2,4-dihydroxybenzylidenyl)-5-(4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10723	E	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5-[4-
10720	-	J	(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10723	E	10	3-(3-bromobenzylidenyl)-5-(4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10723	E	11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyi)-5-[4-
. = 3 = 5	-	, ,	(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
=			
10723	F	2	3-(2,3,4-trihydroxybenzylidenyl)-5-(morpholin-1-
			yl)aminosulfonyl-2-indolinone
10723	F	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5-(morpholin-
	'		1 yl)amınosulfonyl-2-indolinone
	}		
10723	F	4	3-(3-bromo-4,5-dihydroxybenzylidenyi)-5-
			(morpholin-1-yl)amınosulfonyl-2-indolinone
10723	F	5	3-(3,4-diacetoxybenzylidenyl)-5-(morpholin-1-
			yl)aminosulfonyl-2-indolinone
10723	F	6	3-(4-hydroxy-3-methylbenzylidenyl)-5-(morpholin-1-
			yl)aminosulfonyl-2-indolinone
10723	F	7	3-(2-bromobenzylidenyl)-5-(morpholin-1-
	[yl)aminosulfonyl-2-indolinone
10723	F	8	3-(2,4-dihydroxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
			y i/arminosunorryr-z-muomiorre
10723	F	9	3-(2-hydroxy-4-methoxybenzylidenyl)-5-(morpholin-
			1-yl)aminosulfonyl-2-indolinone
10723	F	10	3-(3-bromobenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
			y i/armiosonorry i-z-moomone
L	<u> </u>		

Table 13 (continued)

10723				
		F	11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyl)-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
10723	-	G	2	3-(2,3,4-tnhydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10723		G	3	3-(2-hydroxy-3-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10723		G	4	3-(3-bromo-4,5-dihydroxybenzylidenyl)-5-(2- chloroetnyl)-2-indolinone
10723		G	5	3-(3,4-diacetoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10723		G	6	3-(4-hydroxy-3-methylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10723		G	7	3-(2-bromobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10723		G	8	3-(2,4-dihydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10723		G	9	3-(2-hydroxy-4-methoxybenzyiidenyi)-5-(2- chloroethyl)-2-indolinone
10723	G		10	3-(3-bromobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10723	G		11	3-(3,5-di-t-butyl-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10724	A		2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5,7- dibromo-2-indolinone
10724	A		3	3-(4-hydroxy-3-nitrobenzylidenyl)-5,7-dibromo-2- indolinone
10724	A		4	3-(3-hydroxy-4-nitrobenzylidenyl)-5,7-dibromo-2- indolinone
10724	Α		5	3-[(8-hydroxy-2,3,6,7-tetrahydro-1H,5H-benzo[ij]quinolizin-9-yl)methylidenyl]-5,7-dibromo-2-indolinone
10724	A		6	3-(3,5-diisopropyl-4-hydroxybenzyiidenyl)-5,7- dibromo-2-indolinone

149
Table 13
(continued)

r			
10724	A	7	3-{(benzo(b)furan-2-yi)methylidenyi]-5,7-a.bromo-2- indolinone
10724	A	9	: 3-[[1-(4-chlorophenyl)pyrrol-2-yl]methyliaenyl]-5,7- dibromo-2-indolinone
10724	А	10	3-[(2-ethylfuran-5-yi)methylidenyi]-5,7-dipromp-2- indotinone
10724	A	11	3-[(3,4-dimethylthieno[2,3-b]thien-2-yl)methylidenyl]-5,7-dibromo-2-indolinone
10724	8	2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5-iodo- 2-indolinone
10724	8	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5-iodo-2- indolinone
10724	В	4	3-(3-hydroxy-4-nitrobenzylidenyl)-5-iodo-2- indolinone
10724	В	5	3-[(8-hydroxy-2,3,6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methylidenyl]-5-iodo-2- indolinone
10724	В	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyl)-5-iodo-2- indolinone
10724	В	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5-iodo-2- indolinone
10724	В	9	3-[[1-(4-chloropnenyl)pyrrol-2-yl]methyl:denyl]-5- iodo-2-indolinone
10724	В	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5-iodo-2- indolinone
10724	В	11	3-[(3,4-dimethylthieno[2,3-b]thien-2- yl)methylidenyl]-5-iodo-2-indolinone
10724	С	2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10724	С	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5-bromo-4- methyl-2-indolinone
10724	С	4	3-(3-hydroxy-4-nitrobenzylidenyi)-5-bromo-4- methyl-2-indolinone

C	5	3-[(8-hydroxy-2,3,6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methyl·denyl]-5-bromo-4- methyl-2-indolinone
С	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyl)-5-bromo- 4-methyl-2-indolinone
С	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
С	9	3-[[1-(4-chlorophenyl)pyrrol-2-yl]methylidenyl]-5- bromo-4-methyl-2-indolinone
С	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
С	11	3-[(3,4-dimethylthieno[2,3-b]thien-2-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
Q	2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
D	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	4	3-(3-hydroxy-4-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D .		3-[(8-hydroxy-2,3.6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
D	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
٥	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
D	9	3-[1-(4-chlorophenyl)pyrrol-2-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone
Ď	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
D	11	3-[(3,4-dimethylthieno[2,3-b]thien-2-yl)methylidenyl]-5-methylaminosulfonyl-2-indolinone
Е	2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
		C 6 C 7 C 9 C 10 C 11 D 2 D 3 D 4 D 5

Table 13 (continued)

10724	F		
10724	Ε	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5-(4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	E	4	3-(3-hydroxy-4-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylam:nosulfonyl]-2-indol:none
10724	Ε	5	3-{(8-hydroxy-2,3,6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methylidenyl]-5-{4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	E	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indol:none
10724	E	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	E	9	3-[[1-(4-chlorophenyl)pyrrol-2-yl]methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	Ē	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	E	11	3-[(3,4-dimethylthieno[2,3-b]thien-2- yl)methylidenyi]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10724	F	2	3-{(1-dimethylaminonapth-4-yl)methylidenyl]-5- (morpholin-1yl)aminosulfonyl-2-indolinone
10724	F	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5-(morpholin- 1yl)aminosulfonyl-2-indolinone
10724	F	4	3-(3-hydroxy-4-nitrobenzylidenyl)-5-(morpholin- 1yl)aminosulfonyl-2-indolinone
10724	F	5	3-[(8-hydroxy-2,3,6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methylidenyl]-5-(morpholin- 1yl)aminosulfonyl-2-indolinone
10724	F	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyl)-5- (morpholin-1yl)aminosulfonyl-2-indolinone
10724	F	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5-(morpholin- 1yl)aminosulfonyl-2-indolinone
10724	F	9	3-[[1-(4-chlorophenyl)pyrrol-2-yl]methylidenyl]-5- (morpholin-1yl)aminosulfonyl-2-indolinone
10724	F	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5-(morpholin- 1yl)aminosulfonyl-2-indolinone

152 Table 13 (continued)

40704		,	
10724	F	11	3-[(3,4-dimethylthieno[2,3-b]thien-2- yl)methylidenyl]-5-(morpholin-1yl)aminosulfonyl-2- indolinone
10724	G	2	3-[(1-dimethylaminonapth-4-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10724	G	3	3-(4-hydroxy-3-nitrobenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
10724	G	4	3-(3-hydroxy-4-nitrobenzylidenyi)-5-(2-chloroethyi)- 2-indolinone
10724	G	5	3-[(8-hydroxy-2,3,6,7-tetrahydro-1H,5H- benzo[ij]quinolizin-9-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10724	G	6	3-(3,5-diisopropyl-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10724	G	7	3-[(benzo[b]furan-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10724	G	9	3-[[1-(4-chlorophenyl)pyrrol-2-yl]methylidenyl]-5-(2- chloroethyl)-2-indolinone
10724	G	10	3-[(2-ethylfuran-5-yl)methylidenyl]-5-(2-chloroethyl)- 2-indolinone
10724	G	11	3-[(3,4-dimethylthieno[2,3-b]thien-2-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10725	A	2	3-[(3-bromothien-2-yl)methylidenyl]-5,7-dibromo-2-indolinone
10725	A	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10725	A	4	3-[(2-methylfuran-5-yl)methylidenyl]-5,7-dibromo-2-indolinone
10725	A	5	3-[(3-methylpyrazol-5-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10725	A	6	3-(2-hydroxy-6-methoxy-4-methylbenzylidenyl)-5,7- dibromo-2-indolinone
10725	A	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyl]-5,7- dibromo-2-indolinone

153

Table 13 (continued)

		1 2 // /
A	8	3-[4-(morpholin-1-yi)benzylidenyl]-5.7-dibromo-2- indolinone
А	9	3-[[2-cnioro-4-methoxycarbonyi-3- (methoxycarbonylmethyi)pyrrol-5-yl]methylicenyi]- 5,7-dibromo-4-methyl-2-indolinone
Α	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazol-3-yl]methylidenyl]-5,7-dibromo-4-methyl-2-indol:none
А	11	3-[(imidazol-4-yl)methylidenyl]-5,7-dibromc-4- methyl-2-indolinone
В	2	3-[(3-bromothien-2-yl)methylidenyl]-5-iodo-2- indolinane
В	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyi)-5- iodo-2-indolinone
В	4	3-[(2-methylfuran-5-yl)methylidenyl]-5-ioco-2- indolinone
В	5	3-[(3-methylpyrazol-5-yl)methylidenyl]-5-iodo-2- indolinone
В	6	3-(2-hydroxy-6-methoxy-4-methylbenzylidenyl)-5- iodo-2-indolinone
В	. 7	3-[4-(4-formylpiperaz:n-1-yl)benzylidenyl]-5-iodo-2- indolinone
В	8	3-[4-(morpholin-1-yl)benzylidenyl]-5-iodo-2- indolinone
В	9	3-[[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- iodo-2-indolinone
В	10	3-[[4-broma-2-(4-chlorophenyl)pyrazol-3- yl]methylidenyl]-5-iodo-2-indolinone
8	11	3-[(imidazol-4-yl)methylidenyl]-5-iodo-2-indolinone
С	2	3-[(3-bromothien-2-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
С	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
	A A B B B B B C C	A 9 A 10 A 11 B 2 B 3 B 4 B 5 B 6 B - 7 B 8 B 9 B 10 B 11

154 Table 13 (continued)

10705			
10725	C	4	3-[(2-methylfuran-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10725	C	5	3-[(3-methylpyrazoi-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10725	С	6	3-(2-hydroxy-6-methoxy-4-methylbenzylidenyl)-5- bromo-4-methyl-2-indolinone
10725	С	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyl]-5-bromo- 4-methyl-2-indolinone
10725	С	8	3-[4-(morpholin-1-yl)benzylidenyl]-5-bromo-4- methyl-2-indolinone
10725	C	9	3-{[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- bromo-4-methyl-2-indolinone
10725	С	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazol-3- yl]methylidenyl]-5-bromo-4-methyl-2-indolinone
10725	С	11	3-[(imidazol-4-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10725	D	2	3-[(3-bromothien-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10725	D	-	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10725	D	4	3-[(2-methylfuran-5-yl)metnylidenyl]-5- methylam:nosulfonyl-2-indolinone
10725	D	5	3-[(3-methylpyrazol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10725	D	6	3-(2-hydroxy-6-methoxy-4-methylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10725	D	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10725	D	8	3-[4-(morpholin-1-yl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10725	D	9	3-[[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone

155
Table 13
(continued)

10702		,	
10725	ם -	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazol-3- yl]methylidenyl]-5-methylaminosulfonyl-2-indolinone
10725	D	11	3-[(imidazol-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10725	Ē	2	3-[(3-bromothien-2-yl)methyl/denyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5-[4-(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	4	3-[(2-methylfuran-5-yl)methylidenyi]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	5	3-[(3-methylpyrazol-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	Е	6	3-(2-hydroxy-6-methoxy-4-methylbenzylidenyl)-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
10725	E	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	8	3-[4-(morpholin-1-yl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	. 9	3-[[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2-
10725	Ē	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazol-3- yl]methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	E	11	3-[(imidazol-4-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10725	F	2	3-[(3-bromothien-2-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10725	F	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10725	F	4	3-[(2-methylfuran-5-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10725	F	5	3-{(3-methylpyrazol-5-yl)methylidenyl]-5-(morpholin- 1-yl)sulfonyl-2-indolinone
		<u> </u>	_

156 Table 13 (continued)

46765		·	
10725	F	6	3-(2-hydroxy-6-methoxy-4-methylbenzyl:aenyl)-5- (marpholin-1-yl)sulfonyl-2-indolinone
10725	- F	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10725	F	8	3-[4-(morpholin-1-yl)benzylidenyl]-5-(morpholin-1-yl)sulfonyl-2-indolinone
10725	F	9	3-[[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indol:none
10725	F	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazol-3- yl]methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
10725	F	11	3-[(imidazol-4-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10725	G	2	3-[(3-bromothien-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10725	G	3	3-(2-bromo-6-hydroxy-5-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10725	G	4	3-{(2-methylfuran-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10725	G	5	3-[(3-methylpyrazol-5-yl)methyldenyl]-5-(2- chloroethyl)-2-indolinone
10725	G	6	3-(2-hydroxy-6-methoxy-4-metnyloenzyliaenyl)-5- (2-chloroethyl)-2-indolinone
10725	G	7	3-[4-(4-formylpiperazin-1-yl)benzylidenyi]-5-(2- chloroethyl)-2-indolinone
10725	G	8	3-[4-(morpholin-1-yl)benzylidenyl]-5-(2-chloroethyl)- 2-indolinone
10725	G	9	3-[[2-chloro-4-methoxycarbonyl-3- (methoxycarbonylmethyl)pyrrol-5-yl]methylidenyl]-5- (2-chloroethyl)-2-indolinone
10725	G	10	3-[[4-bromo-2-(4-chlorophenyl)pyrazoi-3- yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone
10725	G	11	3-[(imidazol-4-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone

157
Table 13
(continued)

10726			
10726	Α	3	3-[(2-ethoxycarbonyi-4-methoxycarbonyi-3- methylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2- indolinone
10726	∔ A	4	3-(3-t-butyl-4-hydroxy-5-methylbenzy-ideny!)-5,7- dibromo-2-indolinone
10726	А	5	3-[(2-bromofuran-5-yl)methylidenyl]-5,7-dibromo-2- indolinone
10726	A	6	3-[(1,3-dimethylpyrrol-4-yl)methylidenyl]-5,7- dibromo-2-indolinone
10726	A	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5,7-dibromo-2-indolinone
10726	А	8	3-(5-fluoro-2-oxindol-3-idenyl)-5,7-dibromo-2- indolinone
10726	Ā	9	3-(2-oxindol-3-idenyl)-5,7-dibromo-2-indolinone
10726	A	10	3-[(2-ethylthien-5-yl)methylidenyl]-5,7-dibromo-2- indolinone
10726	A	11	3-(4-methoxybenzylidenyl)-5,7-dibromo-2- indolinone
10726	В	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3-methylpyrrol-5-yl)methylidenyi]-5-iodo-2-indolinone
10726	В	4	3-(3-t-butyl-4-hydroxy-5-methylbenzylidenyl)-5- iodo-2-indol:none
10726	В	5	3-[(2-bromofuran-5-yl)methylidenyl]-5-iodo-2- indolinone
10726	В	6	3-[(1,3-dimethylpyrrol-4-yl)methylidenyl]-5-iodo-2- indolinone
10726	В	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5-iodo-2-indolinone
10726	В	8	3-(5-fluoro-2-oxindol-3-idenyl)-5-iodo-2-indolinone
10726	В	9	3-[(2-oxindol-3-idenyl)methylidenyl]-5-iodo-2- indolinone

158
Table 13
(continued)

10700			
10726	В	10	3-[(2-ethyithien-5-yi)methylidenyi]-5-iodo-2- indolinone
10726	В	11	3-(4-metnoxybenzylidenyl)-5-iodo-2-indolinone
10726	С	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3-methylpyrrol-5-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
10726	С	4	3-(3-t-butyl-4-nydroxy-5-methylbenzylidenyl)-5- bromo-4-methyl-2-indolinone
10726	С	5	3-{(2-bromofuran-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10726	С	6	3-[(1,3-dimethylpyrrol-4-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10726	С	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
10726	С	8	3-(5-fluoro-2-oxindol-3-idenyi)-5-bromo-4-methyl-2- indolinone
10726	С	9	3-(2-axındol-3-idenyl)-5-bromo-4-methyl-2- indolinone
10726	С	10	3-[(2-ethylthien-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10726	С	11	3-(4-methoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10726	D	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3- methylpyrrol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10726	D	4	3-(3-t-butyl-4-hydroxy-5-methylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10726	D	5	3-[(2-bromofuran-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10726	D	6	3-[(1,3-dimethylpyrrol-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10726	D	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5-methylaminosulfonyl-2-indolinone

159 Table 13 (continued)

10726	0		
10720		8	3-(5-fluoro-2-oxindol-3-idenyl)-5-
	:		methylaminosulfonyl-2-indolinone
10726	<u> </u>	9	3-(2-oxindol-3-idenyl)-5-methy/aminosulfonyl-2-
10.20		!	indolinone
			andomione
10726	D	10	3-[(2-ethylthien-5-yl)methylidenyl]-5-
	1		methylaminosulfonyl-2-indolinone
10726	D	11	3-(4-metnoxybenzylidenyl)-5-methylaminosulfonyl-
1	1		2-indolinone
10726	E	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3-
			methylpyrrol-5-yl)methylidenyl]-5-[4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10726	E	4	3-(3-t-butyl-4-hydroxy-5-methylbenzylidenyl)-5-[4-
			(tnfluoromethyl)phenylaminosulfonyl]-2-indolinone
10726	Ε	5	3-[(2-bromofuran-5-yl)methylidenyl]-5-[4-
	ĺ		(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10726	Ε	6	3-[(1,3-dimethylpyrrol-4-yi)methylidenyl]-5-[4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
			,,,
10726	E	7	3-{(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-
			yl)methylidenyl]-5-[4-
	i i		(Influoromethyi)phenylaminosulfonyi]-2-indolinone
10726	E	8	3-(5-fluoro-2-oxindol-3-idenyl)-5-[4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
	1	•	
10726	E	9	3-(2-oxindol-3-idenyl)-5-(4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10726	Ε	10	3-[(2-ethylthien-5-yl)methylidenyl]-5-[4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indotinone
]		
10726	Ε	11	3-(4-methoxybenzylidenyl)-5-(4-
			(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10726	F	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3-
			methylpyrrol-5-yl)methylidenyl]-5-(morpholin-1-
			yl)sulfonyl-2-indolinone
10726	F	4	3-(3-t-butyl-4-hydroxy-5-methylbenzylidenyl)-5-
			(morpholin-1-yl)sulfonyl-2-indolinone
10726	F	5	3-[(2-bromofuran-5-yl)methylidenyl]-5-(morpholin-1-
			yl)sulfonyl-2-indolinone
			

10726	I F		2//2
		6	3-[(1,3-dimethy/pyrrol-4-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10726	F	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
10726	F	8	3-(5-fluoro-2-oxindol-3-idenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10726	F	9	3-(2-oxindol-3-idenyl)-5-(morpholin-1-yl)sulfonyl-2- indolinone
10726	F	10	3-[(2-ethylthien-5-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
10726	F	11	3-(4-methoxybenzyiidenyi)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10726	G	3	3-[(2-ethoxycarbonyl-4-methoxycarbonyl-3-methylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10726	G	4	3-(3-t-butyl-4-hydroxy-5-methylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10726	G	5	3-[(2-bromofuran-5-yi)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10726	G	6	3-[(1,3-dimetnylpyrrol-4-yl)methylidenyi]-5-(2- chloroethyl)-2-indolinone
10726	G	7	3-[(5,8-dihydroxy-1,2,3,4-tetrahydronapth-6-yl)methylidenyl]-5-(2-chicroethyl)-2-indolinone
10726	G	8	3-(5-fluoro-2-oxindol-3-idenyl)-5-(2-chloroethyl)-2- indolinone
10726	G	9	3-(2-oxindol-3-idenyl)-5-(2-chloroethyl)-2-indolinone
10726	G	10	3-{(2-ethylthien-5-yı)methylidenyl]-5-(2-chloroethyl)- 2-indolinone
10726	G	11	3-(4-methoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10727	A	2	3-(4-diethylaminobenzylidenyl)-5,7-dibromo-2- indolinone
	<u>-</u>	·	<u> </u>

161

10727	A	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5.7-dibromo- 2-indolinone
10727	A	4	3-(3-bromo-5-cnlaro-2-hydroxybenzyliaenyl)-5,7- dibromo-2-indolinone
10727	A	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5,7- dibromo-2-indolinone
10727	A	6	3-[(5-chlorobenzodioxolan-6 yl)methylidenyl]-5,7- dibromo-2-indolinone
10727	A	7	3-[(1,4-benzopyranon-3 yl)methylidenyl]-5,7- dibromo-2-indolinone
10727	Ā	8	3-(3-cyanobenzylidenyl)-5,7-dibromo-2-indolinone
10727	A	9	3-(4-cyanobenzylidenyi)-5,7-dibromo-2-indolinone
10727	A	10	3-(2,5-dihydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10727	A	11	3-(2,3-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10727	В	2	3-(4-diethylaminobenzylidenyl)-5-iodo-2-indolinone
10727	8	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5-iodo-2- indolinone
10727	В	4	3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5-iodo- 2-indolinone
10727	В	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5-iodo- 2-indolinone
10727	В	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenyl]-5- iodo-2-indolinone
10727	В	7	3-[(1,4-benzopyranon-3-yl)methylidenyl]-5-iodo-2- indolinone
10727	В	8	3-(3-cyanobenzylidenyl)-5-iodo-2-indolinone

Table 13 (continued)

10727			
	В	9	3-(4-cyanobenzylidenyi)-5-iodo-2-inoolinone
10727	- В	10	3-(2,5-dihydroxybenzylidenyl)-5-iodo-2-indolinone
10727	В	11	3-(2,3-dimethoxybenzylidenyl)-5-iodo-2-indolinone
10727	С	2	3-(4-diethylaminobenzylidenyl)-5-bromo-4-metnyl- 2-indolinone
10727	С	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10727	С	4	3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10727	С	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5- bromo-4-methyl-2-indolinone
10727	С	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10727	C	7	3-[(1,4-benzopyranon-3-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10727	С	8	3-(3-cyanobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10727	С	9	3-(4-cyanobenzylidenyl)-5-bromo-4-methyl-2- indolinone
10727	С	10	3-(2,5-dihydroxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10727	С	11	3-(2,3-dimethoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10727	D	2	3-(4-diethylaminobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10727	D	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10727	D	4	3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
			the same and the s

163 Table 13 (continued)

D	5	3-[2-(4-chlorophenylmercapto)benzylidenylj-5- methylaminosulfonyl-2-indolinone
D	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
D	7	3-[(1,4-benzopyranon-3-yi)methylidenyi]-5- methylaminosulfonyi-2-indolinone
D	8	3-(3-cyanobenzylidenyi)-5-methylaminosuifonyl-2- indolinone
D	9	3-(4-cyanobenzylidenyl)-5-methylaminosulfonyl-2- indolinone
D	10	3-(2,5-dihydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	11	3-(2,3-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
E	2	3-(4-diethylaminobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E		3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5-[4- (tnfluoromethyl)phenylaminosulfonyl]-2-indolinone
E	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	7	3-[(1,4-benzopyranon-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	8	3-(3-cyanobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	9	3-(4-cyanobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	10	3-(2,5-dihydroxybenzylidenyl)-5-[4- (triftuoromethyl)phenylaminosulfonyl]-2-indolinone
	D D D E E E E E	D 6 D 7 D 8 D 9 D 10 D 11 E 2 E 3 E 4 . E 5 E 6 E 7 E 8

164

=	11	3-(2,3-dimethoxycenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
F	2	3-(4-diethylaminobenzylidenyl)-5-(morphol:n-1- yl)sulfonyi-2-indolinone
F	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	4	3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenylj-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	7	3-[(1,4-benzopyranon-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	8	3-(3-cyanobenzylidenyl)-5-(morpholin-1-yl)sulfonyl- 2-indolinone
F	9	3-(4-cyanobenzylidenyl)-5-(morpholin-1-yl)sulfonyl- 2-indolinone
F	10	3-(2,5-dihydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	11	3-(2,3-dimethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
G	2	3-(4-diethylaminobenzylidenyl)-5-(2-chloroetnyl)-2- indolinone
G	3	3-[(2,4-diethylpyrrol-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
G	4	3-(3-bromo-5-chloro-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
G	5	3-[2-(4-chlorophenylmercapto)benzylidenyl]-5-(2- chloroethyl)-2-indolinone
G	6	3-[(5-chlorobenzodioxolan-6-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
	F F G G G	F 2 F 3 F 5 F 6 F 7 F 8 F 9 F 10

Table 13 (continued)

40707			
10727	G	7	3-[(1,4-benzopyranon-3-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10727	G	8	3-(3-cyanobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10727	G	9	3-(4-cyanobenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10727	G	10	3-(2,5-dihydroxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10727	G	11	3-(2,3-dimethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10728	A	2	3-(2,5-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10728	A	3	3-(2,6-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10728	A	4	3-(3,5-dimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10728	A	5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10728	Ä	6	3-{(fluoren-2-yi)methylidenyl]-5,7-dibromo-2- indolinone
10728	A	7	3-[2-fluoro-3-(trifluoromethyl)benzylidenyi]-5,7- dibromo-2-indolinone
10728	A	8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5,7- dibromo-2-indolinone
10728	A	9	3-[2-fluoro-6-(trifluoromethyl)benzylidenyl]-5,7- dibromo-2-indolinone
10728	А	10	3-(2-carboxymethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10728	A	11	3-[(4-methoxybenzodioxolan-6-yl)methylidenyl]-5,7- dibromo-2-indolinone
10728	В	2	3-(2,5-dimethoxybenzylidenyl)-5-iodo-2-indolinone

10728	В	3	3-(2,6-dimethoxybenzylidenyl)-5-iodo-2-indolinone
10728	_ B	4	3-(3.5-dimethoxybenzylidenyl)-5-iodo-2-indolinone
13.23		•	3-(3,3-dimethoxybenzylidenyl)-5-lodo-2-indolinone
10728	В	5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5-iodo-
İ			2-indolinone
10728	B	6	3-[(fluoren-2-yl)methylidenyl]-5-iodo-2-indolinone
10700			
10728	В	7	3-[2-fluoro-3-(trifluorometnyl)benzylidenyl]-5-iodo-2-
			indolinone
10728	В	8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5-iodo-2-
			indolinone
10728	В	9	3-[2-fluoro-6-(trifluoromethyl)benzylidenyl]-5-iodo-2- indolinone
			indollione
10728	В	10	3-(2-carboxymethoxybenzylidenyl)-5-iodo-2-
			indolinone
10728	В	11	3-[(4-methoxybenzodioxolan-6-yl)methylidenyl]-5-
			iodo-2-indolinane
10728	C	2	3-(2,5-dimethoxybenzylidenyl)-5-bromo-4-methyl-2-
			indolinone
10728			
10728	C	3	3-(2,6-dimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
			indoinone
10728	С	4	3-(3,5-dimethoxybenzylidenyl)-5-bromo-4-methyl-2-
			indolinone
10728	- c		
10728		5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
			Status Vindayi Zinidomione
10728	С	6	3-[(fluoren-2-yl)methylidenyl]-5-bromo-4-methyl-2-
			indolinone
10728	c	7	2 (2 8) 2 (4:6)
10720		1	3-[2-fluoro-3-(trifluoromethyl)benzylidenyl]-5-bromo- 4-methyl-2-indolinone
10728	С	8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5-bromo-
			4-methyl-2-indolinone

167
Table 13
(continued)

10728	С	9	3-{2-fluoro-6-(trifluoromethyl)benzylidenyl;-5-bromo- 4-methyl-2-indolinone
10728 _	С	10	3-(2-carboxymethoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10728	С	11	3-[(4-methoxybenzodioxolan-6-yl)methyl.denyl]-5- bromo-4-methyl-2-indolinone
10728	D	2	3-(2,5-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10728	D	3	3-(2,6-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10728	D	4	3-(3,5-dimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10728	D	5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10728	D	6	3-{(fluoren-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10728	D	7	3-[2-fluoro-3-(trifluoromethyl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10728	D	. 8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10728	D	9	3-[2-fluoro-6-(trifluoromethyl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10728	D	10	3-(2-carboxymethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10728	D	11	3-[(4-methoxybenzodioxolan-6-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10728	Ē	2	3-(2,5-dimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10728	E	3	3-(2,6-dimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10728	E	4	3-(3,5-dimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone

E	F	2/4-4
		3-(4-dimethylamino-2-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	6	3-[(fluoren-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	7	3-[2-fluoro-3-(trifluoromethyl)benzylidenyl]-5-[4-(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5-[4-(trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	9	3-[2-fluoro-6-(trifluoromethyl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosuifonyl]-2-indolinone
E	10	3-(2-carboxymethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-[(4-methoxybenzodioxolan-6-yi)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
F	2	3-(2,5-dimethoxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
F	3	3-(2,6-dimethoxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
F	4	3-(3,5-dimethoxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
F	5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
F	6	3-[(fluoren-2-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
F	7	3-[2-fluoro-3-(trifluoromethyl)penzylidenyl]-5- (morpholin-1-yl)amincsulfonyl-2-indolinone
F	8	3-[2-fluoro-5-(trifluoromethyl)benzylidenyl]-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
F	9	3-[2-fluoro-6-(trifluoromethyl)benzylidenyl]-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
F	10	3-(2-carboxymethoxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
	E E F F	E 6 E 7 E 8 E 9 E 10 E 11 F 2 F 3 F 4 F 5 F 6 F 7

Table 13 (continued)

10728	F	11	3-[(4-methoxybenzodioxolan-6-yl)methylidenyl]-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
10728 _	G	2	3-(2,5-dimethoxybenzylidenyi)-5-(2-chloroethyi)-2- indolinone
10728	G	3	3-(2,6-dimethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10728	G	4	3-(3,5-dimethoxybenzylidenyl)-5-(2-chloroethyl)-2- indolinone
10728	G	5	3-(4-dimethylamino-2-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10728	G	6	3-[(fluoren-2-yl)methylidenyl]-5-(2-cnloroethyl)-2- indolinone
10728	G	7	3-[2-fluoro-3-(trifluoromethyl)benzylidenyl]-5-(2- chloroethyl)-2-indolinone
10728	G	8	3-[2-fluoro-5-(trifluoromethyi)benzylidenyi]-5-(2- chloroethyi)-2-indolinone
10728	G	9	3-[2-fluoro-6-(trifluoromethyl)penzylidenyl]-5-(2- chloroethyl)-2-indolinone
10728	G	10	3-(2-carboxymethoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10728	G	11	3-[(4-methoxybenzodioxolan-6-yl)methylidenyl]-5- (2-chloroethyl)-2-indolinone
10729	A	2	3-{(2-methoxynapth-1-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10729	A	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10729	A	4	3-(4-methylmercaptobenzylidenyl)-5,7-dibromo-2- indolinone
10729	A	5	3-[(3-methylth:en-2-yl)methylidenyl]-5,7-dibromo-2- indolinone
10729	A	6	3-(3-phenoxybenzylidenyl)-5,7-dibromo-2- indolinone
			and the control of th

170

10729	1	,	
	A	7	3-[(pyrid-2-yl)methylidenyl]-5,7-dibromo-2- indolinone
10729	- A	8	3-[(pyrid-3-yl)methylidenyl]-5,7-dibromo-2- indolinone
10729	A	9	3-[(pyrid-4-yl)methylidenyl]-5,7-dibromo-2- indolinone
10729	A	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5,7-dibromo-2- indolinone
10729	A	11	3-[(cyclohexen-3-yl)methylidenyl]-5,7-dibromo-2- indolinone
10729	В	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-iodo-2- indolinone
10729	В	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5-iodo-2- indolinone
10729	В	4	3-(4-methylmercaptobenzylidenyl)-5-iodo-2- indolinone
10729	В	5	3-[(3-methylthien-2-yl)methylidenyl]-5-iodo-2- indolinone
10729	В	6	3-(3-phenoxybenzylidenyl)-5-iodo-2-indolinone
10729	В	7	3-[(pyrid-2-yl)methylidenyl]-5-iodo-2-indolinone
10729	В	8	3-[(pyrid-3-yl)methylidenyl]-5-iodo-2-indolinone
10729	В	9	3-[(pyrid-4-yl)methyliaenyl]-5-iodo-2-indolinone
10729	В	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-iodo-2- indolinone
10729	В	11	3-[(cyclohexen-3-yl)methylidenyl]-5-iodo-2- indolinone
10729	С	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone

10729	C	3	3-[(1-methoxynapth-4-yl)methylicnyl]-5-bromo-4- methyl-2-indolinone
10729	С	4	3-(4-methylmercaptobenzylidenyi)-5-bromo-4- methyl-2-indolinone
10729	С	5	3-[(3-methylthien-2-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10729	С	6	3-(3-phenoxybenzylidenyl)-5-bromo-4-methyl-2- indolinone
10729	С	7	3-[(pyrid-2-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10729	С	8	3-{(pyrid-3-yl)methylidenyi}-5-bromo-4-methyl-2- indolinone
10729	С	9	3-[(pyrid-4-yl)methylidenyl]-5-bromo-4-methyl-2- indolinane
10729	С	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-bromo-4- methyl-2-indolinone
10729	С	11	3-{(cyclohexen-3-yl)methylidenyl}-5-bromo-4- methyl-2-indolinone
10729	D	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D		3-[(1-methoxynapth-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D	4	3-(4-methylmercaptobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10729	D	5	3-{(3-methylthien-2-yl)methyldenyl}-5- methylaminosulfonyl-2-indolinone
10729	D	6	3-(3-phenoxybenzylidenyl)-5-methylaminosulfonyl- 2-indolinone
10729	D	7	3-[(pyrid-2-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone
10729	D	8	3-[(pyrid-3-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone

172 Table 13 (continued)

A	8 9	3-[(pynd-2-yi)methylidenyi]-5,7-dibromo-2- indolinone 3-[(pyrid-3-yi)methylidenyi]-5,7-dibromo-2- indolinone 3-[(pyrid-4-yi)methylidenyi]-5,7-dibromo-2- indolinone
А	9	indolinone 3-[(pyrid-4-yl)methylidenyl]-5,7-dibromo-2-
А	10	
	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5,7-dibromo-2- indolinone
А	11	3-[(cyclohexen-3-yl)methylidenyl]-5,7-dibromo-2- indolinone
8	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-iodo-2- indolinone
В	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5-iodo-2- indolinone
В	4	3-(4-methylmercaptobenzylidenyi)-5-iodo-2- indolinone
В	5	3-[(3-methylthien-2-yl)methylidenyl]-5-iodo-2- indolinone
В	6	3-(3-phenoxybenzylidenyl)-5-iodo-2-indolinone
В	7	3-[(pyrid-2-yl)methylidenyl]-5-iodo-2-indolinone
В	8	3-{(pyrid-3-yl)methyliaenyl]-5-ioao-2-indolinane
В	9	3-[(pyrid-4-yl)methylidenyl]-5-iodo-2-indolinone
В	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-iodo-2- indolinone
В	11	3-[(cyclohexen-3-yl)methylidenyl]-5-iodo-2- indolinone
С	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
	B B B B B B B	A 11 B 2 B 3 B 4 B 5 B 6 . B 7 B 8 B 9 B 10 B 11

173
Table 13
(continued)

10729	С	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10729 _	С	4	3-(4-methylmercaptobenzylidenyl)-5-bromo-4- methyl-2-indolinone
10729	С	5	3-[(3-methylthien-2-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10729	С	6	3-(3-phenoxybenzylidenyl)-5-bromo-4-metnyl-2- indolinone
10729	С	7	3-[(pyrid-2-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10729	С	8	3-[(pyrid-3-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10729	С	9	3-[(pyrid-4-yl)methylidenyl]-5-bromo-4-methyl-2- indolinone
10729	С	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-bromo-4- methyl-2-indolinone
10729	С	11	3-{(cyclohexen-3-yl)methylidenyl}-5-bromo-4- methyl-2-indolinone
10729	D	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D	4	3-(4-methylmercaptobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10729	D	5	3-[(3-methyithien-2-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D	6	3-(3-phenoxybenzylidenyl)-5-methylaminosulfonyl- 2-indolinone
10729	D	7	3-[(pyrid-2-yl)methylidenyl]-5-methylaminosulfonyl- 2-indol:none
10729	D	8	3-{(pyrid-3-yl)methylidenyl}-5-methylaminosulfonyl- 2-indolinone

174 Table 13 (continued)

10729			
10729	D	9	3-[(pynd-4-yl)methylidenyl]-5-methylaminosulfonyl- 2-indolinone
10729	D	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	D	11	3-[(cyclohexen-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10729	E	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	4	3-(4-methylmercaptobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	5	3-[(3-methylthien-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	6	3-(3-phenoxybenzylidenyl)-5-(4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	Ε	7	3-[(pyrid-2-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	8	3-[(pyrid-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	Ē	9	3-[(pyrid-4-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	E	11	3-[(cyclohexen-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10729	F	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
10729	F	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5- (morpholin-1-yl)aminosulfonyl-2-indolinone
10729	F	4	3-(4-methylmercaptobenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone

175 Table 13 (continued)

10729	F	5	3-[(3-methylth:en-2-yl)methylidenyl]-5-(morphoin-1-yl)aminosulfonyl-2-indolinone
10729	F	6	3-(3-phenoxybenzylidenyl)-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10729	F	7	3-[(pyrid-2-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10729	F	8	3-{(pyrid-3-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10729	F	9	3-{(pyrid-4-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10729	F	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-(morpholin-1- yl)aminosuifonyl-2-indolinone
10729	F	11	3-[(cyclohexen-3-yl)methylidenyl]-5-(morpholin-1- yl)aminosulfonyl-2-indolinone
10729	G	2	3-[(2-methoxynapth-1-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10729	G	3	3-[(1-methoxynapth-4-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10729	G	4	3-(4-methylmercaptopenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10729	G	5	3-[(3-methylthien-2-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10729	G	6	3-(3-phenoxybenzylidenyl)-5-(2-chloroetnyl)-2- indolinone
10729	G	7	3-[(pyrid-2-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone
10729	G	8	3-[(pyrid-3-yI)methylidenyI]-5-(2-chloroethyI)-2- indolinone
10729	G	9	3-[(pyrid-4-yl)methylidenyl]-5-(2-chloroethyl)-2- indolinone
10729	G	10	3-[4-(pyrrolidin-1-yl)benzylidenyl]-5-(2-chloroethyl)- 2-indolinone

176
Table 13
(continued)

40720			
10729	G	11	3-[(cyclohexen-3-yl)methylidenyl]-5-(2-ch.oroethyl)- 2-indolinone
10730	- A	2	3-(2,3,4-trimethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10730	A	3	3-(2,4.5-tnmethoxybenzylidenyl)-5,7-dibromo-2- indolinone
10730	A	4	3-(3,4,5-trimethoxyoenzylidenyl)-5,7-dibromo-2- indolinone
10730	A	5	3-[(1-acetylindol-3-yl)methylidenyl]-5,7-dipromo-2-indolinone
10730	A	6	3-[(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]- 5,7-dibromo-2-indolinone
10730	A	7	3-[2-[(2-chlorophenyi)furan-5-yl]methylidenyi]-5,7- dibromo-2-indolinone
10730	A	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10730	A	9	3-[(6,8-dibromo-1,4-benzofuranon-3- yl)methylidenyl]-5,7-dibromo-2-indolinone
10730	A	10	3-[(2,5-dimethoxytetrahydrofuran-3- yl)methylidenyl]-5,7-dibromo-2-indolinone
10730	A	11	3-{(2,3-dimethylfuran-5-yl)methylidenyl]-5,7- dibromo-2-indolinone
10730	В	2	3-(2,3,4-trimethoxybenzylidenyl)-5-iodo-2- indolinone
10730	В	3	3-(2,4,5-trimethoxybenzylidenyl)-5-iodo-2- indolinane
10730	8	4	3-(3,4,5-trimethoxybenzylidenyl)-5-iodo-2- indolinone
10730	В	5	3-[(1-acetylindol-3-yl)methylidenyl]-5-iodo-2- indolinone
10730	В	6	3-{(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5-iodo-2-indolinone
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177

Table 13 (continued)

10730	ТВ	7	2/2//
		7	3-[2-[(2-chloroprienyl)furan-5-yl]methylidenyi]-5- iodo-2-indolinone
10730	В	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5-iodo-2- indolinone
10730	В	9	3-[(6,8-dibromo-1,4-benzoturanon-3- yl)methylidenyl]-5-iodo-2-indolinone
10730	В	10	3-[(2,5-dimethoxytetrahydrofuran-3-yl)methylidenyl]-5-iodo-2-indolinone
10730	В	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5-iodo-2- indolinone
10730	С	2	3-(2,3,4-trimethoxybenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10730	С	3	3-(2,4,5-trimethoxybenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10730	С	4	3-(3,4,5-trimethoxybenzylidenyl)-5-bromo-4-methyl- 2-indolinone
10730	С	5	3-[(1-acetylindol-3-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10730	С	. 6	3-[(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone
10730	С	7	3-[2-[(2-chlorophenyl)furan-5-yı]methylidenyl]-5- bromo-4-methyl-2-indolinone
10730	С	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10730	С	9	3-[(6,8-dibromo-1,4-benzofuranon-3- yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
10730	С	10	3-[(2,5-dimethoxytetrahydrofuran-3-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
10730	С	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10730	Ď	2	3-(2,3,4-trimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
			

178
Table 13
(continued)

10730	i D	·	
10730		3	3-(2,4,5-trimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10730	D	4	3-(3,4,5-trimethoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10730	D	5	3-[(1-acetylindol-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10730	D	6	3-[(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10730	D	7	3-[2-[(2-chlorophenyl)furan-5-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone
10730	D	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10730	D	9	3-[(6,8-dibromo-1,4-benzofuranon-3- yl)methylidenyl]-5-methylaminosulfonyl-2- indolinone
10730	D	10	3-[(2,5-dimethoxytetrahydrofuran-3- yl)methylidenyl]-5-methylaminosulfonyl-2- indolinone
10730	D	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10730	Ε	2	3-(2,3,4-trimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10730	E	3	3-(2,4,5-trimethoxybenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10730	E	4	3-(3.4,5-trimethoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10730	Е	5	3-[(1-acetylindol-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10730	E	6	3-{(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
10730	E	7	3-[2-[(2-chlorophenyl)furan-5-yl]methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10730	E	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone

179
Table 13
(continued)

Ш	9	3-[(6,8-dibromo-1,4-benzofuranon-3-yl)methylidenyl]-5-[4-(tnfluoromethyl)phenylaminosulfonyl]-2-indolinone
E	10	3-[(2,5-dimethoxytetrahydrofuran-3- yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
F	2	3-(2,3,4-tnmethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	3	3-(2,4,5-tnmethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	4	3-(3,4,5-trimethoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	5	3-[(1-acetylindol-3-yl)methylidenyl]-5-(morpholin-1- yl)sulfonyl-2-indolinone
F	6	3-[(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	7	3-[2-[(2-chiorophenyl)furan-5-yl]methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinane
F	8	3-[(2-chlorcquinolin-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	9	3-[(6,8-dibromo-1,4-benzofuranon-3- yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
F	10	3-[(2,5-dimethoxytetrahydrofuran-3- yl)methylidenyl]-5-(morpholin-1-yl)sulfonyl-2- indolinone
F	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
G	2	3-(2,3,4-trimethoxybenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
G	3	3-(2,4,5-trimethoxybenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
G	4	3-(3,4,5-trimethoxybenzylidenyl)-5-(2-chloroethyl)- 2-indolinone
	E F F F F G G	E 10 E 11 F 2 F 3 F 6 F 7 F 8 - F 9 F 10 F 11 G 2 G 3

Table 13 (continued)

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10730	G	5	3-[(1-acetylindol-3-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10730	G	6	3-[(6-chloro-1,4-benzofuranon-3-yl)methylidenyl]-5- (2-chloroethyl)-2-indolinone
10730	G	7	3-[2-[(2-chlorophenyl)furan-5-yl]methylidenyl]-5-(2- chloroethyl)-2-indolinone
10730	G	8	3-[(2-chloroquinolin-3-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10730	G	9	3-[(6,8-dibromo-1,4-benzofuranon-3-yl)methylidenyl]-5-(2-chloroethyl)-2-indoinone
10730	G	10	3-[(2,5-dimethoxytetrahydrofuran-3- yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
10730	G	11	3-[(2,3-dimethylfuran-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10731	A	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10731	A	3	3-[(6,7-dimethyl-1,4-benzopyron-3-yl)methylidenyl]- 5,7-dibromo-2-indolinone
10731	A	4	3-[[4-(propen-2-yl)cyclonexen-1-yl]methylidenyi]- 5,7-dibromo-2-indolinone
10731	A	5	3-{(6-isopropyl-1,4-benzopyron-3-yl)methylidenyl]- 5,7-dibromo-2-indolinone
10731	A	6	3-{(6-methyl-1,4-benzopyron-3-yi)methylidenyi]-5,7-dibromo-2-indolinone
10731	A	7	3-[(6-nitro-1,4-benzopyron-3-yl)methylidenyl]-5,7- dibromo-2-indolinone
10731	A	8	3-[(pyrimid-2,4-dion-5-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10731	A	9	3-[(5-methoxyindol-3-yl)methylidenyl]-5,7-dibromo- 2-indolinone
10731	A	10	3-(1-methyl-2-oxindol-3-idenyl)-5,7-dibromo-2- indolinone

181
Table 13
(continued)

10731	A	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5,7- dibromo-2-indolinone
10731	В	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5-iodo-2- indolinone
10731	8	3	3-[(6,7-dimethyl-1,4-benzopyron-3-yl)methylidenyl]- 5-iodo-2-indolinone
10731	В	4	3-[[4-(propen-2-yl)cyclohexen-1-yl]methylidenyl]-5- iodo-2-indolinone
10731	8	5	3-[(6-isopropyi-1,4-benzopyron-3-yl)methylidenyi]- 5-iodo-2-indolinone
10731	8	6	3-[(6-methyl-1,4-benzopyron-3-yl)methylidenyl]-5- iodo-2-indolinone
10731	В	7	3-[(6-nitro-1,4-benzopyron-3-yl)methylidenyl]-5- iodo-2-indolinone
10731	В	8	3-[(pyrimid-2,4-dion-5-yl)methylidenyl]-5-iodo-2- indolinone
10731	8	9	3-[(5-methoxyindal-3-yl)methylidenyl]-5-iada-2- indalinane
10731	8	10	3-(1-methyl-2-oxindol-3-idenyl)-5-iodo-2-indolinane
10731	В	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5-iodo- 2-indolinone
10731	С	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone
10731	С	3	3-{(6,7-dimethyl-1,4-benzopyran-3-yl)methylidenyl}- 5-bromo-4-methyl-2-indolinone
10731	С	4	3-[[4-(propen-2-yl)cyclohexen-1-yl]methylidenyl]-5- bromo-4-methyl-2-indolinone
10731	С	5	3-[(6-isopropyl-1,4-benzopyron-3-yl)methylidenyl]- 5-bromo-4-methyl-2-indolinone
10731	С	6	3-{(6-methyl-1,4-benzopyron-3-yl)methylidenyl]-5- bromo-4-methyl-2-indolinone

Table 13 (continued)

10731	С	7	3-[(6-nitro-1,4-benzopyron-3-yl)methylidenyi]-5- bromo-4-methyl-2-indolinone
10731	С	8	3-[(pyrimid-2,4-dion-5-ylimethylidenyl]-5-bromo-4- methyl-2-indolinone
10731	C	9	3-[(5-methoxyindol-3-yi)methylidenyi]-5-bramo-4- methyl-2-indolinane
10731	С	10	3-(1-methyl-2-oxindol-3-idenyl)-5-bromo-4-methyl- 2-indolinone
10731	С	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5- bromo-4-methyl-2-indolinone
10731	D	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	3	3-[(6,7-dimethyl-1,4-benzopyron-3-yl)methylidenyl]- 5-methylaminosulfonyl-2-indolinone
10731	D	4	3-[[4-(propen-2-yl)cyclohexen-1-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	5	3-[(6-isopropyl-1,4-benzopyron-3-y!)methylidenyl]- 5-methylaminosulfonyl-2-indolinone
10731	D	6	3-[(6-methyl-1,4-benzopyron-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	7	3-[(6-nitro-1,4-benzopyron-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	8	3-[(pyrimid-2,4-dion-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	9	3-[(5-methoxyindol-3-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	D	10	3-(1-methyl-2-oxindol-3-idenyl)-5- methylaminosulfonyl-2-indolinone
10731	D	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5- methylaminosulfonyl-2-indolinone
10731	E	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone

Table 13 (continued)

E	3	3-1/6 7-dimothyl 1 4 honzanisan 3 the
		3-[(6,7-dimetnyl-1,4-benzopyron-3-yl)methylidenyl]- 5-[4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinone
E	4	3-[[4-(propen-2-yl)cyclohexen-1-yl]methylidenyl]-5- [4-(tnfluoromethyl)phenylaminosulfonyl]-2- indolinone
E	5	3-{(6-isopropyl-1,4-benzopyron-3-yl)methylidenyl}-5-{4-(trifluoromethyl)phenylaminosulfonyl}-2-indolinone
E	6	3-[(6-methyl-1,4-benzopyron-3-yl)methylidenyl]-5- [4-(trifluoromethyl)phenylaminosulfonyl]-2- indolinane
E	7	3-{(6-nitro-1,4-benzopyron-3-yl)methylidenyl]-5-{4- (tnfluoromethyl)phenylaminosulfonyl]-2-indolinone
E	8	3-[(pyrimid-2,4-dion-5-yl)methylidenyl]-5-[4- (tnfluoromethyl)phenylaminosulfonyl]-2-indolinone
E	9	3-[(5-methoxyindol-3-yl)methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	10	3-(1-methyl-2-oxindol-3-idenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
F	2	3-[(9-ethylcarbazol-3-yl)methylidenyl]-5-(morpholin- 1-yl)sulfonyl-2-indolinone
F	3	3-[(6,7-dimethyl-1,4-benzopyron-3-yl)methylidenyl]- 5-(morpholin-1-yl)sulfonyl-2-indolinane
F	4	3-[[4-(propen-2-yl)cyclohexen-1-yl]methylidenyl]-5- (morpholin-1-yl)sulfanyl-2-indolinane
F	5	3-[(6-isopropyl-1,4-benzopyron-3-yl)methylidenyl]- 5-(morpholin-1-yl)sulfonyl-2-indolinone
F	6	3-[(6-methyl-1,4-benzopyron-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinane
F	7	3-[(6-nitro-1,4-benzopyron-3-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
F	8	3-[(pyrimid-2,4-dion-5-yl)methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
		E 5 E 6 E 7 E 8 E 9 E 10 E 11 F 2 F 3 F 6 F 7

Table 13 (continued)

40724			
10731	F	9	3-[(5-methoxyindol-3-yl)methylideny!]-5-(morpholin- 1-yl)sulfonyl-2-indolinone
10731 _	F	10	3-(1-methyl-2-oxindol-3-idenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10731	F	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
10731	G	2	3-{(9-ethylcarbazol-3-yl)methylidenyl}-5-(2- chloroethyl)-2-indolinone
10731	G	3	3-[(6,7-dimethyl-1,4-benzopyron-3-yl)methylidenyl]- 5-(2-chloroethyl)-2-indolinone
10731	G	4	3-[[4-(propen-2-yi)cyclohexen-1-yi]methyiidenyi]-5- (2-chloroethyi)-2-indolinone
10731	G	5	3-[(6-isopropyi-1,4-benzopyron-3-yi)methylidenyi]- 5-(2-chloroethyl)-2-indolinone
10731	G	6	3-[(6-methyl-1.4-benzopyron-3-yl)methylidenyl]-5- (2-chloroethyl)-2-indolinone
10731	G	7	3-[(6-nitro-1,4-penzopyron-3-yl)methylidenyl]-5-(2- chloroethyl)-2-indalinone
10731	G	8	3-[(pynmid-2,4-dion-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone
10731	G	9	3-[(5-methaxyindal-3-yl)methylidenyl]-5-(2- chloraethyl)-2-indalinane
10731	G	10	3-(1-methyl-2-oxindol-3-idenyl)-5-(2-chloroetnyl)-2-indolinone
10731	G	11	3-[2-[2-(nitrophenyl)furan-5-yl]methylidenyl]-5-(2- chloroethyl)-2-indolinone
10732	A	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5,7- dibromo-2-indolinone
10732	A	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10732	A	4	3-(3,5-diisopropyl-4-phenoxybenzylidenyl)-5,7- dibromo-2-indolinone
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185
Table 13
(continued)

10720	· · · · · · · · · · · · · · · · · · ·		
10732	А	5	3-(3-t-butyl-4-methoxybenzylidenyl)-5,7-a;bromo-2- indolinone
10732 _	Α	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5,7-dibromo- 2-indollnone
10732	Α	7	3-(3-bromo-5-t-butyl-4-methoxypenzylidenyi)-5,7- dibromo-2-indolinone
10732	A	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5,7- dibromo-2-indolinane
10732	A	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10732	A	10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyl)-5,7- dibromo-2-indolinone
10732	A	11	3-(3-t-butyl-5-iodo-4-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10732	В	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5- iodo-2-indolinane
10732	В	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5-iodo-2- indolinone
10732	В	4	3-(3,5-diisopropyl-4-phenoxybenzylidenyl)-5-iodo-2- indolinone
10732	8	5	3-(3-t-butyl-4-methoxybenzylidenyl)-5-iodo-2- indolinane
10732	В	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5-iodo-2- indolinone
10732	В	7	3-(3-bromo-5-t-butyl-4-methoxybenzylidenyl)-5- iodo-2-indolinone
10732	В	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5- iodo-2-indolinone
10732	В	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5- iodo-2-indolinone
10732	В	10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyl)-5- iodo-2-indolinone
L			<u></u>

186
Table 13
(continued)

10732		-,	
	В	11	3-(3-t-butyl-5-iodo-4-methoxybenzylidenyl)-5-iodo- 2-indolinone
10732 _	С	2	3-[2-(thien-2-yl)-2-(tnfluoromethyl)ethylidenyl]-5- bromo-4-methyl-2-indolinone
10732	С	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	4	3-(3,5-diisopropyl-4-phenoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	5	3-(3-t-butyl-4-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10732	С	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5-bromo-4- methyl-2-indolinone
10732	С	7	3-(3-bromo-5-t-butyl-4-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	. 10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyl)-5- bromo-4-methyl-2-indolinone
10732	С	11	3-(3-t-butyi-5-iodo-4-methoxybenzylidenyi)-5- bromo-4-methyl-2-indolinone
10732	D	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5- methylaminosulfonyl-2-indolinone
10732	D	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10732	Ď	4	3-(3,5-disopropyl-4-phenoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10732	D	5	3-(3-t-butyl-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10732	D	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone

187 Table 13 (continued)

D	7	3-(3-bromo-5-t-butyl-4-methoxybenzyl:denyt)-5- methylaminosulfonyl-2-indolinone
D	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
D	11	3-(3-t-butyl-5-iodo-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
E	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
Е	4	3-(3,5-diisopropyl-4-phenoxybenzylideny)]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	5	3-(3-t-bulyl-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indoiinone
E	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	7	3-(3-bromo-5-t-butyl-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl}-2-indolinone
Ε	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
Ē	10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
E	11	3-(3-t-butyl-5-iodo-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
F	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5- (morpholin-1-yl)sulfonyl-2-indolinone
	D D D E E E E	D 8 D 9 D 10 D 11 E 2 E 3 E 4 E 5 E 6 - 7 E 8 E 9 E 10

188
Table 13
(continued)

10732		, , , , , , , , , , , , , , , , , , , 	
	F	3	3-(3,5-diisopropyl-4-methoxybenzyl:denyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732 _	F	4	3-(3,5-disopropyl-4-phenoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	F	5	3-(3-t-butyl-4-methoxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10732	F	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5-(morpholin- 1-yl)sulfonyl-2-indolinone
10732	F	7	3-(3-bromo-5-t-butyl-4-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	F	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	F	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	F	10	3-(4-benzyloxy-5-t-butyl-3-chloro-benzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	F	11	3-(3-t-butyl-5-iodo-4-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10732	G	2	3-[2-(thien-2-yl)-2-(trifluoromethyl)ethylidenyl]-5-(2-chloroethyl)-2-indolinone
10732	G	3	3-(3,5-diisopropyl-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10732	G	4	3-(3,5-diisopropyl-4-phenoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10732	G	5	3-(3-t-butyl-4-methoxybenzylidenyi)-5-(2- chloroethyl)-2-indolinone
10732	G	6	3-(4-benzyloxy-3-t-butylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10732	G	7	3-(3-bromo-5-t-butyl-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10732	G	8	3-(4-benzyloxy-3-bromo-5-t-butylbenzylldenyl)-5-(2-chloroethyl)-2-indolinone

189
Table 13
(continued)

10732	7 6		
	G	9	3-(3-t-butyl-5-chloro-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10732	G	10	3-(4-benzyloxy-5-t-butyl-3-chlorobenzylidenyl)-5-(2- chloroethyl)-2-indolinane
10732	G	11	3-(3-t-outyl-5-iodo-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	A	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5,7- dibromo-2-indolinone
10733	A	3	3-(3-t-butyl-4-methoxy-5-nitrobenzyliaenyi)-5,7- dibromo-2-indolinone
10733	A	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5,7- dibromo-2-indolinone
10733	A	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyl)-5,7- dibromo-2-indolinone
10733	A	6	3-(3,5-dimethyl-4-methoxypenzylidenyl)-5,7- dibromo-2-indolinone
10733	A	7	3-(4-benzyloxy-3,5-dimethylbenzylidenyl)-5,7- dibromo-2-indolinone
10733	A	. 8	3-(5-bromo-2-hydroxy-3-methoxybenzyiidenyl)-5,7- dibromo-2-indolinone
10733	A	9	3-(5-bromo-2-hydroxypenzylidenyl)-5,7-dibromo-2- indolinone
10733	A	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5,7-dibroma-2- indolinone
10733	A	11	3-(4-hydroxy-3-methoxy-2-nitrobenzyliaenyl)-5,7- dibromo-2-indolinone
10733	В	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5-iodo- 2-indolinone
10733	8	3	3-(3-t-butyl-4-methoxy-5-nitrobenzylidenyl)-5-iodo- 2-indolinone
10733	8	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5-iodo-2- indolinone
	 		

190 Table 13 (continued)

40722			
10733	В	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyl)-5-iodo-2- indolinone
10733 _	8	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5-iodo-2- indolinone
10733	В	7	3-(4-benzyloxy-3,5-aimethylbenzylidenyl)-5-iodo-2- indolinone
10733	В	8	3-(5-promo-2-hydroxy-3-methoxypenzylideny!)-5- iodo-2-indolinone
10733	8	9	3-(5-bromo-2-hydroxybenzylidenyl)-5-iodo-2- indolinone
10733	8	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5-iodo-2- indolinone
10733	8	11	3-(4-hydroxy-3-methoxy-2-nitrobenzylidenyl)-5- iodo-2-indolinone
10733	С	2	3-(4-benzyloxy-3-t-butyi-5-iodobenzylidenyi)-5- bromo-4-methyl-2-indolinone
10733	С	3	3-(3-t-butyl-4-methoxy-5-nitrobenzylidenyl)-5- bromo-4-methyl-2-indolinone
10733	С	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10733	С	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyl)-5-bromo- 4-methyl-2-indolinone
10733	С	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10733	С	7	3-(4-benzyloxy-3,5-dimethylbenzylidenyl)-5-bromo- 4-methyl-2-indolinone
10733	С	8	3-(5-bromo-2-hydroxy-3-methoxybenzylidenyl)-5- bromo-4-methyl-2-indolinone
10733	С	9	3-(5-bromo-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
10733	С	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5-bromo-4- methyl-2-indolinone

191 Table 13 (continued)

10733	С	11	3-(4-hydroxy-3-methoxy-2-nitrobenzylidenyl)-5- bromo-4-methyl-2-indolinone
10733 _	D	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	3	3-(3-t-butyl-4-methoxy-5-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	7	3-(4-benzyloxy-3,5-dimethylbenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	8	3-(5-bromo-2-hydroxy-3-methoxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	9	3-(5-bromo-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5- methylaminosulfonyl-2-indolinone
10733	D	11	3-(4-hydroxy-3-methoxy-2-nitrobenzylidenyi)-5- methylaminosulfonyl-2-indolinone
10733	ξ	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	3	3-(3-t-butyl-4-methoxy-5-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
			

192 Table 13 (continued)

10733	E	7	2/4
		/	3-(4-benzyloxy-3,5-dimethylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	8	3-(5-bromo-2-hydroxy-3-methoxybenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	ε	9	3-(5-bromo-2-hydroxybenzylidenyi)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	E	11	3-(4-hydroxy-3-methoxy-2-nitrobenzylidenyi)-5-{4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10733	F	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	3	3-(3-t-butyl-4-metnoxy-5-nitropenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	5	3-(4-benzyloxy-3,5-di-t-butylbenzylidenyt)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	7	3-(4-benzyloxy-3,5-dimethylbenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	8	3-(5-bromo-2-hydroxy-3-methoxybenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	F	9	3-(5-bromo-2-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10733	F	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10733	F	11	3-(4-hydroxy-3-methoxy-2-nitrobenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10733	G	2	3-(4-benzyloxy-3-t-butyl-5-iodobenzylidenyl)-5-(2- chloroethyl)-2-indolinone
			<u> </u>

193
Table 13
(continued)

10733	G	3	3-(3-t-butyl-4-methoxy-5-nitrobenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	G	4	3-(3,5-di-t-butyl-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	G	5	3-(4-Denzyloxy-3,5-di-t-butylbenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	G	6	3-(3,5-dimethyl-4-methoxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	G	7	3-(4-benzyloxy-3,5-dimethylbenzyliaenyi)-5-(2- chloroethyl)-2-indolinone
10733	G	8	3-(5-bromo-2-hydroxy-3-methoxybenzyliaenyl)-5- (2-chloroethyl)-2-indolinone
10733	G	9	3-(5-bromo-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone
10733	G	10	3-(2-hydroxy-5-nitrobenzylidenyl)-5-(2-chtoroethyl)- 2-indolinone
10733	G	11	3-(4-hydroxy-3-methoxy-2-nitrobenzyliaenyl)-5-(2- chloroethyl)-2-indolinone
10734	Α	2	3-(3-ethoxy-2-hydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10734	A	3	3-(3,5-dichloro-2-hydroxybenzyliaenyl)-5,7- dibromo-2-indolinone
10734	A	4	3-(5-chloro-2-hydroxybenzylidenyl)-5,7-dibromo-2- indolinone
10734	A	5	3-(4-diethylamino-2-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10734	A	6	3-(4-nitrobenzylidenyl)-5,7-dibromo-2-indolinone
10734	Α	7	3-(3,5-dibromo-2-hydroxybenzylidenyl)-5,7- dibromo-2-indolinone
10734	A	8	3-(3-fluoro-2-hydroxybenzylidenyl)-5,7-dibromo-2- indolinone
			

194 Table 13 (continued)

10734	10734	i A	9	2 /2 5:00
10734			9	3-(3-bromo-4-hydroxybenzylidenyl)-5, 7-dibromo-2- indolinone
10734 B 3 3-(3-ethoxy-2-hydroxybenzylidenyl)-5-iodo-2- indolinone	10734 _	A	10	3-(4-t-butylbenzylidenyl)-5,7-dibromo-2-indolinone
10734 B 3 3-(3,5-dichloro-2-hydroxybenzylidenyl)-5-iodo-2- indolinone	10734	A	11	
10734 B 3-(3-fluoro-2-hydroxybenzylidenyl)-5-iodo-2-indolinone	10734	В	2	
10734 B 5 3-(4-diethylamino-2-hydroxybenzylidenyl)-5-iodo-2-indolinone	10734	В	3	
10734 B 6 3-(4-nitrobenzylidenyl)-5-iodo-2-indolinone	10734	8	4	
10734 B 7 3-(3,5-dibromo-2-hydroxybenzylidenyl)-5-iodo-2-indolinone	10734	В	5	3-(4-diethylamino-2-hydroxybenzylidenyl)-5-iodo-2- indolinone
10734 B 8 3-(3-fluoro-2-hydroxybenzylidenyl)-5-iodo-2-indolinone	10734	В	6	3-(4-nitrobenzylidenyl)-5-iodo-2-indolinone
10734 B 9 3-(3-bromo-4-hydroxybenzylidenyl)-5-iodo-2-indolinone	10734	В	7	
10734 B 10 3-(4-t-butylbenzylidenyl)-5-iodo-2-indolinone	10734	В	8	
10734 B 11 3-[(2-bromothien-5-yl)methylidenyl]-5-iodo-2-indolinone 10734 C 2 3-(3-ethoxy-2-hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 10734 C 3 3-(3,5-dichloro-2-hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone	10734	В	9	
indolinone 10734	10734	В	10	3-(4-t-butylbenzylidenyl)-5-iodo-2-indolinone
10734 C 4 3-(5-chloro-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone	10734	В	11	
methyl-2-indolinone 10734 C 4 3-(5-chloro-2-hydroxybenzylidenyl)-5-bromo-4-	10734	С	2	
- 1 (10734	С	3	3-(3,5-dichloro-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone
	10734	С	4	

195
Table 13
(continued)

10734	С	5 3-(4-diethylamino-2-hydroxybenzylidenyl)-5-bromo- 4-methyl-2-indolinone		
1030			,	
10734 _	C	6	3-(4-nitrobenzylidenyl)-5-bromo-4-metny -2- indolinone	
10734	С	7	3-(3,5-dibromo-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone	
10734	С	8	3-(3-fluoro-2-hydroxybenzylidenyl)-5-bromo-4- methyl-2-indolinone	
10734	С	9	3-(3-bromo-4-hydroxybenzyildenyi)-5-bromo-4- methyl-2-indolinone	
10734	С	10	3-(4-t-buty/benzyl/aenyl)-5-bromo-4-metnyl-2- indolinone	
10734	С	11	3-[(2-bromothien-5-yl)methylidenyl]-5-bromo-4- methyl-2-indolinone	
10734	D	2	3-(3-ethoxy-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	3	3-(3,5-dichloro-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	4	3-(5-chloro-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indoknone	
10734	D	5	3-(4-diethylamino-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	6	3-(4-nitrobenzylidenyl)-5-methylaminosulfonyl-2- indolinone	
10734	D	7	3-(3,5-dibromo-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	8	3-(3-fluoro-2-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	9	3-(3-bromo-4-hydroxybenzylidenyl)-5- methylaminosulfonyl-2-indolinone	
10734	D	10	3-(4-t-butylbenzylidenyl)-5-methylaminosulfonyl-2- indolinone	

196 Table 13 (continued)

10734		1 44	
10734	D	11	3-[(2-promothien-5-yl)methylidenyl]-5- methylaminosulfonyl-2-indolinone
10734 _	E	2	3-(3-etnoxy-2-hydroxybenzylidenyl)-5-[4- (trifluorometnyl)phenylaminosulionyl]-2-indolinone
10734	E	3	3-(3,5-dichloro-2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosuifonyl]-2-indolinone
10734	E	4	3-(5-chloro-2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	Ë	5	3-(4-diethylamino-2-hydroxypenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	Ε	ô	3-(4-nitrobenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	E	7	3-(3,5-dibromo-2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	E	8	3-(3-fluoro-2-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	E	9	3-(3-bromo-4-hydroxybenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	E	10	3-(4-t-butylbenzylidenyl)-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
10734	É	11	3-[(2-bromothien-5-yi)metnylidenyl]-5-[4- (trifluoromethyl)phenylaminosulfonyl]-2-indolinone
16734	F	2	3-(3-ethoxy-2-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10734	F	3	3-(3,5-dichlora-2-hydroxybenzylidenyl)-5- (morphalin-1-yl)sulfonyl-2-indalınane
10734	F	4	3-(5-chloro-2-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone
10734	F	5	3-(4-diethylamino-2-hydroxypenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone
10734	F	6	3-(4-nitrobenzylidenyl)-5-(morpholin-1-yl)sulfonyl-2- indolinone

197 Table 13 (continued)

10734	F	7	3-(3.5-dibromo-2-hydroxypenzylidenyl)-5- (morpholin-1-yl)sulfonyl-2-indolinone	
10734	F	8	3-(3-fluoro-2-nydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone	
10734	F	9	3-(3-bromo-4-hydroxybenzylidenyl)-5-(morpholin-1- yl)sulfonyl-2-indolinone	
10734	F	10	3-(4-t-butylbenzylidenyl)-5-(morpholin-1-yl)sulfanyl- 2-indolinone	
10734	F	11		
10734	G	2	3-(3-ethoxy-2-hydroxypenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	3	3-(3,5-dichloro-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	4	3-(5-chloro-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	5	3-(4-diethylamino-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	-	3-(4-nitrobenzylidenyl)-5-(2-chioroethyl)-2- indolinone	
10734	G	7	3-(3,5-dibromo-2-hydroxypenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	8	3-(3-fluoro-2-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	9	3-(3-bromo-4-hydroxybenzylidenyl)-5-(2- chloroethyl)-2-indolinone	
10734	G	10	3-(4-t-butylbenzylidenyl)-5-(2-chloroethyl)-2- indol:none	
10734	G	11	3-[(2-bromothien-5-yl)methylidenyl]-5-(2- chloroethyl)-2-indolinone	

Table 14

Barcode/	Fik Kinase	Biochem EGFR	ODCC	I Mat Kinasa
Plate Row-	rik Kinase	Blochem EGFK	PDGF	Met Kinase
Plate Column			Kinase	
Plate Column	%Inhibition	%Inhibition	%Inhibition	! % Inhibition
10717/A02	0.1	24.3	70111110111011	46.1
10717/A03	2.9	1.0	-	54.6
10717/A04	-4.5	29.0		37.4
10717/A05	-2.6	16.6		35.6
10717/A06	-10.8	-7.8		31.7
10717/A07	-6.4	20.2		29.2
10717/A08	-5.2	39.1		21.7
10717/A09	-3.9	37.7		9.4
10717/A10	-3.3	8.1		71.6
10717/A11	-5.8	59.9	···	64.8
10717/B02	5.0	31.7		87.5
10717/B03	-8.8	7.3		90.5
10717/B04	-18.3	10.3		70.0
10717/B05	1.0	31.7		87.4
10717/B06	5.4	-30.8		89.5
10717/B07	-18.3	58.3		90.0
10717/B08	-0.9	60.5		88.8
10717/B09	-40.7	78.3		88.8
10717/B10	-2.3	16.1		56.1
10717/B10	11.4	82.7		91.0
10717/C02	4.1	-0.4		29.7
10717/C03	-7.7	18.0		
10717/C03	-0.8	14.4		25.3 25.0
10717/C05	-2.3	13.1		
10717/C05	7.6	-49.7		44.6
10717/C08		28.7		44.1
10717/C08	1.6			16.5
10717/C09	7.0 · 77.1	24.3		27.3
	-8.0	8.1 17.5		47.7
10717/C10 10717/C11				22.8
10717/D02	4.6 5.1	67.3		71.8
10717/D02	1.1	10.1		286
10717/D03		-1.4		11 1
10717/D04	-2.1 -3.8	4.9		21 0
10717/D05		-2.8 -23.4		23.8
	1.0			33.8
10717/D07 10717/D08	-8.4	-4.5 7.9		16.8
10717/D08	6.8	-7.8		16.0
10717/D09	-55.0	6.8		29.1
10717/D10	-6.0	3.5		15.6
10717/E02	11.6	59.1		55.3
	17.9 19.0	17.2		24.0
10717/E03 10717/E04		11.7		52.2
10717/E04	6.1	-28.3		29.4
	13.2	22.4		39.1
10717/E06	7.5	-26.1		24.8
10717/E07	15.3	-7.8		41.0
10717/E08	13.2	28.2		51.7
10717/E09	-1.1	-5.8		19.2
10717/E10	4.7	-6.1		35.9
10717/E11	8.9	44.9		75.1

199
Table 14
(continued)

10717/F02	2.2		
	2.2	6.2	30.4
10717/F03	0.5	-4.7 -15.7	42.8
10717/F04	-0.1	-13.7	11 4
10717/F05	3.2	-20.1	21.5
10717/F06	8.9	-22.8	49.0
10717/F07	2.0	-14.3	37.6
10717/F08	-0.7	-23.4	64 0
10717/F09	-13.3	1.8	41.4
10717/F10	-4.4	-26.4	54.6
10717/F11	1.4	91.2	81.5
10717/G02	14.9	32.3	30.7
10717/G03	1.8	18.8	4.5
10717/G04	0.8	6.0	10.9
10717/G05	5.3	-0.1	4.7
10717/G06	4.3	-3.4	34.0
10717/G07	-17.0	13.1	7.5
10717/G08	1.9	36.4	10.9
10717/G09	-29.7	24.9	19.1
10717/G10	4.8	2.4	30.9
10717/G11	16.4	71.7	73.8
10718/A02	3.0	11.3	54.6
10718/A03	7.6	-6.1	92.7
10718/A04	6.9	27.3	81.7
10718/A05	3.2	-6.9	36.1
10718/A06	7.8	19.4	61.3
10718/A07	16.2	-10.6	58.6
10718/A08	3.2	5.8	
10718/A09	-18.4	-4.1	67.7
10718/A10	23.4	41.5	77.9
10718/A11	2.7	21.2	58.9
10718/B02	7.0.	24.9	52.9
10718/B03	1.7	-0.2	77.9
10718/B04	11.8	8.5	63.9
10718/B05	11.5	56.3	76.0
10718/B06	16.5	28.5	78.4
10718/B07	17.7	9.9	53.7
10718/B08	5.4	28.9	63.4
10718/B09	-14.7	-0.8	52.9
10718/B10	20.1	13.7	83.6
10718/B10	4.5	30.3	69.6
10718/C02	26.2	-21.9	29.6
10718/C02	-13.9		95.7
10718/C04	15.3	41.3	93.1
10718/C05	20.5	10.9	8.7
10718/C06 10718/C07	16.8	5.6	3.9
	6.3	-4.9	29.6
10718/C08	19.6	13.1	22.7
10718/C09	5.3	26.5	38.2
10718/C10	-11.9	-18.7	4.4
10718/C11	11.4	-0.2	10.1
10718/D02	13.3	14.4	32.0
10718/D03	1.1	61.9	92.9
10718/D04	6.4	52.0	92.9
10718/D05	11.5	2.8	10.6

200 Table 14 (continued)

10718/D06	15.8	20.0	11.1
10718/D07	7.8	5.6	; 26.1
10718/D08	3.9	3.0	2.3
10718/D09	-9.1	6.0	9.9
10718/D10	15.0	12.3	55.3
10718/D11	13.3	5.4	113
10718/E02	19.7	1.0	46.3
10718/E03	10 0	50.4	95.3
10718/E04	15.1	16.4	87.7
10718/E05	16.1	-3.1	32 2
10718/E06	15.4	2.0	33 4
10718/E07	15.6	13.9	80 5
10718/E08	9.2	9.3	69.6
10718/E09	0.9	17.0	80.8
10718/E10	15.2	-7.5	60 8
10718/E11	12.1	-15.2	37 5
10718/F02	20.1	17.8	66.7
10718/F03	-0.2	22.5	879
10718/F04	9.4	1,2	78.1
10718/F05	19.5	-4.9	53.7
10718/F06	18.3	-9.1	42.5
10718/F07	16.5	-6.3	67.9
10718/F08	15.3	-8.7	28.4
10718/F09	-3.0	-9.5	52.7
10718/F10	17.9	-12.0	23.7
10718/F11	10.1	-3.9	31.3
10718/G02	-2.5	49.2	67.7
10718/G03	-4.7	57.3	77.9
10718/G04	1.8	15.8	78.1
10718/G05	3.7	2.8	60 3
10718/G06	9.8	-18.7	61.0
10718/G07	11.4	-21.3	52.0
10718/G08	6.1	-8.3	17.5
10718/G09	-12.8	-15.4	27 0
10718/G10	7.1	-7.5	! 108
10718/G11	15.6	-4.9	3.0
10719/A02	21.4	43.0	40 9
10719/A03	3.9	67.7	84.1
10719/A04	19.2	43.7	22.9
10719/A05	10.0	23.1	39.6
10719/A06	14.0	18.2	-7.0
10719/A07	21.3	15.5	68.1
10719/A08	11.9	47.3	75 5
10719/A09	12.3	2.2	47 0
10719/A10	10.9	8.2	13.4
10719/A11	7.4	10.5	47.0
10719/B02	11.5	29.0	85.8
10719/B03 10719/B04	14.2	59.5 29.9	38 4
10719/B04 10719/B05	24.9		33.6
10719/B05	17.7 21.3	35.9	22.5
10719/B05			52.2
10719/B07	12.5	23.7 42.3	33 2
10719/B08 10719/B09	4.0	-17.7	23.5
101 19/809	11.3	-17.7	23.3

Table 14 (continued)

10719/B10	1.1	-1.2	53.4
10719/B11	11.2	-23 9	36.5
10719/C02	4.1	10.2	41.3
10719/C03	15.3	60.6	69.1
10719/C03	59.9	14.4	14.7
10719/C04	25.6	27.4	35.5
10719/C05	47.7	-14 3	
10719/C03	31.2	14.4	7.7
10719/C08	15.0	-10.2	57.5
10719/C08	23.5	-0.1	
10719/C10	11.8	10.7	8.9 7.9
10719/C10	9.9	-25.7	
10719/D02	9.9		-5.1
		9.8	27.5
10719/D03	4.8	95.7	93.2
10719/D04	27.8	15.3	28.9
10719/D05	16.3	18.5	71.8
10719/D06	25.8	-12.2	11.2
10719/D07	-123.5	13.7	41.5
10719/D08	8.2		45.2
10719/D09	7.8	-3.1	13.0
10719/D10	8.3	-11.8	22.3
10719/D11	-8.7	-11.1	12.8
10719/E02	26.1	40.0	35.7
10719/E03	17.1	73.0	87.2
10719/E04	31.2	-7.4	3.1
10719/E05	21.5	21.2	39.0
10719/E06	17.1	-42.0	-4.5
10719/E07	26.7	-18.4	55.5
10719/E08	21.8	36.8	80.0
10719/E09	13.5	-33.1	36.1
10719/E10	17.6	-32.4	40.2
10719/E11	26.3	-51.8	28.5
10719/F02	28.5	14.8	28.1
10719/F03	11.2	-30.8	89.5
10719/F04	26.6	-6.0	3.3
10719/F05	20.7	35.0	63.1
10719/F06	13.5	-26.0	-22.0
10719/F07	18.7	20.1	36.7
10719/F08	15.1	90.9	75.7
10719/F09	-6.5	-17.7	19.2
10719/F10	10.4	-17.7	30.8
10719/F11	11.6	-66.3	8.7
10719/G02	27.3	-12.2	-2.4
10719/G03	-25.8	89.5	87.6
10719/G04	11.5	-4.7	-8.2
10719/G05	18.0	4.0	15.9
10719/G06	23.2	-45.7	-18.1
10719/G07	20.1	-8.1	24.0
10719/G08	3.2	65.4	39.4
10719/G09	18.1	-32.8	1.3
10719/G10	9.7	-27.6	35.5
10719/G11	6.9	-44.1	24.0
10720/A02	4.7	11 3	45.2
10720/A03	17.7	-5.3	58.2
101201700	1 17.7		

202 Table 14 (continued)

10720/A05	10720/A04	. 12.3	-1.8	62.3
10720/A06				
10720/A07 66 42.5 57.2 10720/A08 -2.2 -2.3.2 77.9 10720/A09 8.1 8.6 75.4 10720/A10 -5.2 -2.7 68.4 10720/A11 -0.6 -2.3.2 58.7 10720/B02 6.5 18.4 38.8 10720/B03 6.4 32.3 53.3 10720/B03 6.4 32.3 53.3 10720/B04 9.8 50.5 61.8 10720/B05 11.6 58.4 51.8 10720/B05 11.6 58.4 51.8 10720/B05 7.3 21.2 55.1 10720/B08 3.6 -12.6 27.7 10720/B08 3.6 -12.6 27.7 10720/B09 10.1 37.6 57.4 10720/B10 -5.5 50.2 45.2 10720/B11 -20.3 22.4 42.1 10720/C02 18.0 23.5 63.6 10720/C03 15.1 0.9 50.3 10720/C04 15.3 -13.1 29.0 10720/C04 15.3 -13.1 29.0 10720/C05 -36.1 -15.3 72.5 10720/C07 20.7 -25.4 26.7 26.7 10720/C09 12.1 44.7 47.5 10720/C09 12.1 44.7 47.5 10720/C09 12.1 44.7 47.5 10720/C09 12.1 11.1 17.8 10720/C09 12.1 11.1 17.8 10720/C09 12.1 11.1 17.8 10720/C09 12.1 14.4 14.8 36.2 10720/C09 3.3 -13.3 42.1 10720/C09 3.3 -13.3 42.1 39.8 10720/C09 3.3 -13.3 3.3 42.1 39.8 10720/C09 3.3 -13.3 3.3 42.1 39.8 10720/C09 3.3 -13.3 3.3 42.1 39.8 36.2 30.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 31.8 36.2 30.0 30.		0.0	<u> </u>	
10720/A08			 	
10720/A09				
10720/A10			·	
10720/A11				
10720/B02 6.5				
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10720/B06				
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10720/C02				
10720/C03		20.0		
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10720/C05 -36.1 -15.3 72.5 10720/C06 12.2 -9.7 36.7 10720/C07 20.7 -25.4 26.7 10720/C08 10.9 -1.1 65.6 10720/C09 12.1 44.7 47.5 10720/C10 -21.1 2.0 62.6 10720/C01 52.5 -21.9 30.0 10720/C02 12.1 11.1 17.8 10720/D02 12.1 11.1 17.8 10720/D03 17.0 0.9 61.5 10720/D03 17.0 0.9 61.5 10720/D04 15.6 -7.7 23.6 10720/D05 4.8 -24.1 9.8 10720/D05 4.8 -24.1 9.8 10720/D06 10.1 -35.0 31.8 10720/D07 11.8 14.8 36.2 10720/D08 3.3 -13.3 42.1 10720/D09 5.8 2.4 62.8 10720/D09 5.8 2.4 62.8 10720/D09 5.8 2.4 62.8 10720/D10 -6.6 -10.2 51.0 10720/E02 5.7 25.2 18.0 10720/E03 34.3 54.4 54.9 10720/E04 18.4 -2.7 46.7 46.7 10720/E05 -13.8 40.7 55.4 10720/E06 25.5 30.1 33.1 10720/E07 18.8 55.1 30.3 10720/E08 2.5 37.4 55.1 10720/E08 2.5 37.4 55.1 10720/E08 2.5 37.4 55.1 10720/E09 11.5 56.4 43.4 10720/E09 11.5 56.4 43.4 10720/E09 11.5 56.4 43.4 10720/E09 11.5 56.4 43.4 10720/E09 11.5 56.4 43.4 10720/E07 9.1 -19.3 17.8 10720/F03 10.6 7.1 44.1 10720/F04 10.6 -11.7 43.1 10720/F05 -3.6 -14.2 39.8 10720/F06 11.9 -24.3 21.9				
10720/C06				
10720/C07			<u> </u>	
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10720/C10 -21.1 2.0 62.6 10720/C11 52.5 -21.9 30.0 10720/D02 12.1 11.1 17.8 10720/D03 17.0 0.9 61.5 10720/D04 15.6 -7.7 23.6 10720/D05 4.8 -24.1 9.8 10720/D06 10.1 -35.0 31.8 10720/D07 11.8 14.8 36.2 10720/D08 3.3 -13.3 42.1 10720/D09 5.8 2.4 62.8 10720/D10 -6.6 -10.2 51.0 10720/E01 9.8 -5.5 23.9 10720/E02 5.7 25.2 18.0 10720/E03 34.3 54.4 54.9 10720/E03 34.3 54.4 54.9 10720/E04 18.4 -2.7 46.7 10720/E05 -13.8 40.7 55.4 10720/E06 25.5 30.1 33.1 10720/E08				
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10720/F03 10.6 7.1 44.1 10720/F04 10.6 -11.7 43.1 10720/F05 -3.6 -14.2 39.8 10720/F06 11.9 -24.3 21.9				
10720/F04 10.6 -11.7 43.1 10720/F05 -3.6 -14.2 39.8 10720/F06 11.9 -24.3 21.9				
10720/F05 -3.6 -14.2 39.8 10720/F06 11.9 -24.3 21.9	10720/F04			
10720/F06 11.9 -24.3 21.9	10720/F05			
	10720/F06			
10/40/FU/ ! 4.6 35.2 1 64.6	10720/F07	4.6	35.2	64.6

Table 14 (continued)

10720/F08	-4.1	-39.6	36 2
10720/F09	5.9	6.4	49.2
10720/F10	-2.6	6.0	42 8
10720/F11	5 0	-61.1	1.6
10720/G02	5 0	-13.1	20 1
10720/G03	2 6	10.0	42.1
10720/G04	2.4	-34.1	5.0
10720/G05	-2.9	27.0	37 0
10720/G06	-3.4	-10.4	216
10720/G07	5 1	-8.0	12.9
10720/G08	-17.9	-9.5	26.7
10720/G09	2.1	-19.7	49.5
10720/G10	-36.6	20.4	55.9
10720/G11	-18.0	-56.7	36.2
10721/A02	10.6	17.8	41.1
10721/A03	11.4	25.5	56 2
10721/A04	6.5	59.0	85.0
10721/A05	12.5	41.4	52.9
10721/A06	6.4	32.7	81 3
10721/A07	-4.7	35.2	29 7
10721/A08	4 8	24.0	29.9
10721/A09	10.9	28.0	23.0
10721/A10	5.2	31.1	68.9
10721/A11	4.8	24.6	23.9
10721/B02	19.5	58.6	82.6
10721/B03	19.9	38.9	70.8
10721/B04	13.8	79.3	93.1
10721/B05	45.9	76.8	70.8
10721/B06	3.4	71.5	92.4
10721/B07	11.2	47.6	47.1
10721/B08	18.5	64.0	64 5
10721/B09	9.0	38.9	28.3
10721/B10	20.9	42.9	30.4
10721/B11	-2.1	34.6	6.7
10721/C02	9 7	68.3	59.2
10721/C03	16.5	64.6	6.2
10721/C04	21.8	77.7	88.7
10721/C05	56.4	68.1	48.7
10721/C06	14.4	80.2	56.4
10721/C07	10.9	24.6	25.7
10721/C08	55.8	38.3	24.8
10721/C09	17.5	39.8	-4.7
10721/C10	21.1	17.4	44.6
10721/C11	13.9	14.1	3.7
10721/D02	15.1	21.5	22.5
10721/D03	17.8	11.6	19.5
10721/D04	15.2	5.0	35.3
10721/D05	-25.1	47.0	91.9
10721/D06	1.6	44.5	9.0
10721/D07	6.4	23.0	-6.8
10721/D08	3.9	31.7	45.3
10721/D09	17.6	15.3	-4.9
10721/D10	23.7	3.3	13.4
10721/D11	20.6	22.2	23.2

204 Table 14 (continued)

10721/E02	17.2	-9.5		200
10721/E03	10.9	25.1		38.8
10721/E04	16.0			12.3
10721/E05	10.8	48.5	 	87.3
10721/E06	40.4	91.5		69.9
10721/E07	15.6	37.7		81.0
10721/E08	15.7	29.8	 	43.6
10721/E09	36.9	42.5	 	39.5
10721/E10	9.3	19.9	ļ	0.7
10721/E11	0.7	32.1		+
10721/F02	17.0	11.0		31.3
10721/F03	9.1	7.0	 	27.8 40.6
10721/F04	7.4	0.0	 	1 26.0
10721/F05	8.1	20.5	-	67.8
10721/F06	2.2	21.7	 	80.3
10721/F07	4.8	3.5	 	55.7
10721/F08	-6.4	37.3	 	76.1
10721/F09	65.2	7.0	 	52.5
10721/F10	49.6	7.5	 	79.9
10721/F11	29.7	95.9	 	78.2
10721/G02	16.4	23.6	 	7.9
10721/G03	12.1	23.4		25.3
10721/G04	3.2	64.6	 	90.3
10721/G05	-15.1	7.7	 	8.6
10721/G06	18.9	23.2	 	39.5
10721/G07	3.3	14.7		10.0
10721/G08	5.4	12.8	 	-2.4
10721/G09	20.4	14.9		5.1
10721/G10	24.4	2.1		12.0
10721/G11	-7.1	0.4	 	-0.0
10722/A02	0.8 -	23.7	28.9	44.9
10722/A03	6.7	0.8	29.5	90.3
10722/A04	13.4	21.0	-0.9	51.4
10722/A05	10.5	22.4	33.5	90.5
10722/A06	9.6	28.4	19.8	71.6
10722/A07	9.4	29.9	23.8	64.1
10722/A08	13.7	23.9	15.2	70.5
10722/A09	7.3	16.8	21.5	86.5
10722/A10	6.6	-4.2	15.2	79.0
10722/A11	6.7	-0.1	21.5	68.6
10722/B02	10.1	16.3	28.9	44.3
10722/B03	13.6	19.6	3.7	40.1
10722/B04	14.7	10.6	3.1	53.4
10722/B05	18.5	9.3	21.5	67.2
10722/B06	13.9	-4.9	21.5	72.6
10722/B07	6.6	6.2	20.9	48.2
10722/B08 10722/B09	11.2	0.5	27.8	72.0
10722/B09 10722/B10	8.7	7.8	14.6	59.7
10722/B10	-0.9	-11.3	20.3	56.4
10722/C02	5.2 29.1	-15.5 32.1	25.5 30.6	83.0 34.5
10722/C02	16.7	42.3	22.6	73.6
10700.00	10.7	26.7	8.9	70.7
10722/C05	23.5	19.1	26.6	44.9
	40.0	1.7.1	20.0	77.9

Table 14 (continued)

10722/C06	24.5	-11 0	24 9	45.1
10722/C07	15.8	-15.5	31 2	61.2
10722/C08	17.8	14.8	31.2	80.1
10722/C09	25.9	-3.1	32.4	45.1
10722/C10	2.3	22.8	18.0	
10722/C11	13.8	-14 2	36.4	
10722/002	30.7	26.1	31.8	
10722/003	15.0	31.0	-94	52.8
10722/D04	23.5	20.3	15.7	
10722/D05	21.4	-3.8	22.0	35.8
10722/D06	21.9	-2.5	8.9	32 4
10722/D07	14.1	-2.8	25.5	42 6
10722/D08	29.1	-2.6	41.5	60.5
10722/D09	14.7	-17.2	30.6	52.2
10722/D10	8.2	-0.6	41.5	40.5
10722/D11	9.6	-10.1	15 2	41 0
10722/E02	17.0	22.2	23 2	71 1
	10.7	33.0	-7.2	88 4
10722/E04	38.6	1.4	30.6	52 6
10722/E05	19.2	-7.0	19.2	73 0
10722/E06	21.4	7.6	32.9	71.6
10722/E07	24.3	28.7	40.9	71.6
10722/E08	18.6	10.4	38.7	82.8
10722/E09	16.2	4.1	26.6	55.1
10722/E10	3.1	-13.3	31.8	86.6
10722/E11	15.3	4.2	28.3	84.0
10722/F02	5.3	9.2	12.9	33.9
10722/F03	12.0	13.7	-14.0	59.7
10722/F04	27.5	16.8	-2.0	58.9
10722/F05	15.0	-2.8	6.0	6.4
10722/F06	11.0	6.5	2.6	6.0
10722/F07	15.5	-3.7	-6.6	63.0
10722/F08	66.3	-5.4	25.5	89.3
10722/F09	15.3	-35.8	26.6	65.7
10722/F09	3.3	10.7		67.8
10722/F10	3.3 4.5		15.7	
10722/G02		-6.5 27.3		73.2
10722/G02	15.1	4.1	14 6	43.0 52.2
10722/G03	5.3 7.2	-13.3	-3.7	63.2
10722/G04	10.8		-6.0	9.7
10722/G05	7.4	-9.0 -5.2	-6.0 -6.0	12.2
10722/G07	8.0	-32.5	-3.7	41.2
10722/G07				
	8.2	-8.5	12 9	66 1
10722/G09	6.1	-5.9	0.9	51.0
10722/G10	-1.7	3.3	16.9	27 0
10722/G11	0.6	-39.4	0.3	35.3
10723/A02	-5.5	97.8	64.4	100.8 76.5
10723/A03	1.2	38.5	11.7	
10723/A04	27.2	30.8	13.1	97.9
10723/A05	-17.8	26.4	17.9	75.7
10723/A06	8.6	20.1	43.6	79.1
10723/A07	-6.1	3.9	22.1	63 2
10723/A08	-12.9 j	-2.1	29.7	77.3
10723/A09	-1.0	-4.5	42.9	85.9

206 Table 14 (continued)

10723/A10	-3.1	-24 8	34.6	62.1
10723/A11	42.9	-4.0	41.5	60.0
10723/B02	-0.3	91,0	29.0	100.3
10723/B03	7.1	-5.0	14.5	82.5
10723/B04	18 7	5.1	40.4	90.6
10723/805	-15.4	36.4	15.2	85.1
10723/B06	31.8	11.9	58.8	
10723/B07	6.5	28.8	24.9	86.7
10723/B08	1.0	-0.4	56.1	82.8
10723/B09	2.7	-12.0	27 6	
10723/810	5.8	1.8	17.2	88.5
10723/B11	6.3	-26.0		62.6
10723/C02	9.6	73.6	39.4	100.6
10723/C03	-3.1	5.9	42.9	88.8
10723/C04	8.8	23.5	36.7	91.9
10723/C05	5.6	35.2	22.8	72.4
10723/C06	17.8	-4.5	26.3	63.4
10723/C07	20.9	-4.0	27.6	
10723/C08	-35.5	45.0	29.0	83.0
10723/C09	-22.3	62.7	62.3	84.6
10723/C10	9.5	-7.2	25.6	43.8
10723/C11	9.5	-1.1	8.9	47.0
10723/D02	2.0	63.2	22.1	93.0
10723/D03	-14.7	33.5	8.2	69.4
10723/D04	15.2	45.1	31.8	97.7
10723/D05	-6.1	3,7	8.2	54.5
10723/D06	17.6	-7.4	6.2	60.0
10723/D07	15.8	13.4	16.6	21.9
10723/D08	-4.5	4.9	31.1	53.5
10723/D09	50.4	-3.8	21.4	62 6
10723/D10	6.5	-9.3	21.4	38 1
10723/D11	14.8	-6.2	24.9	42 0
10723/E02	8.1	91.0	46.4	97.9
10723/E03	8.7	8.3	47.1	76 8
10723/E04	30.7	59.8	36.0	94.5
10723/E05	8.9	-15.6	-4.9	63.7
10723/E06	19.3	11.5	18.6	74 4
10723/E07	17.4	38.1	14.5	47 7
10723/E08	-0.4	52.6	26.3	89 3
10723/E09	7.9	29.1	22.1	91.7
10723/E10	5.2	-7.9	44.3	59 5
10723/E11	8.9	-44.6	32.5	50.1
10723/F02	10.3	70.4	1.3	99 0
10723/F03	4.4	9.3	13	78 3
10723/F04	12.3	17.5	21.4	94 0
10723/F05	-6.4	-3.8	-7.7	45 6
10723/F06	20.4	5.4	-30.6	84.1
10723/F07	20.7	-4.1	6.8	26.6
10723/F08	-0.5	5.7	20.7	75 5
10723/F09	1.2	14.1	3.4	78.6
10723/F10	9.1	4.2	-2.2	74.1
10723/F11	-1.2	-41.3	36.7	72.3
10723/G02	-1.6	90.8	13.8	99.2
10723/G03	4.3	18.5	6.2	74.7

Table 14 (continued)

10723/G04 I	8.7	16.7	21.4	85.9
10723/G04 10723/G05	-9.4	1.3	2.0	79.9
10723/G05		-26.7		64.5
	14.1			
10723/G07	14.2	15.5	-5.6	43.0
10723/G08	-22.9	0.1	7.5	79.9
10723/G09	-1.8	-32.6	-2.9	80.7
10723/G10	. 3.5	-4 1	-27.8	40.7
10723/G11	-4.1	-35.0	-7 7	39.4
10724/A02	1.8	36.7	6.3	61 7
10724/A03	-7.8	17.2	0.1	30.7
10724/A04	-15.9	15.4	5.0	62.6
10724/A05	-15.2	20.3	5.0	68.4
10724/A06	-3.7	1.4	30.7	46.8
10724/A07	3.7	18.3	16.1	58.7
10724/A09	-5.2	1.6	19.6	37.5
10724/A10	1.6	40.0	28.6	83.8
10724/A11	12.8	-16.6	29.3	27.2
10724/B02	-6.2	34.9	-21.5	48.8
10724/B03	-48.9	14.9	14.7	51.0
10724/B04	-20.5	50.2	42.5	81.2
10724/B05	-2.2	21.2	12.6	45.6
10724/B06	13.4	30.9	43.2	52.1
10724/807	-1.8	44.0	27.2	57.9
10724/B09	3.5	8.7	25.8	43.8
10724/B10	8.5	76.2	9.8	95.0
10724/B11	9.0	-23.2	23.0	43.0
10724/C02	-0.3	53.6	-9.0	40.7
10724/C03	-20.3	16.5	4.3	68.7
10724/C04	-18.6	13.2	24.4	84.3
10724/C05	-18.6	-0.8	20.3	67.7
10724/C06	-1.5	-2.4	34.9	15.4
10724/C07	-1.2	9.4	22.3	14.2
10724/C09	9.3	1.0	20.3	5.3
10724/C10	-2,3	13.8	27.2	91.2
10724/C11	10.3	0.7	23.0	4.9
10724/D02	12.4	40.5	-9.6	37.5
10724/D03	0.1	2.5	-15.2	18.2
10724/D03	0.5	5.4	-1.3	70.5
10724/D05	-1.6	-8.4	35.6	36.1
10724/D05	12.4	-12.4	40.4	23.0
10724/D07	-2.6	25.6	7.0	38.1
10724/D07	0.9	-15.3	18.9	16.1
10724/D10	3.7	12.7	38.3	59.6
	14.9	12.9	29.3	20.3
10724/D11 10724/E02	17.7	39.8	-54.2	55.4
10724/E02	10.6	33.1	14.7	85.8
10724/E03	5 5 .2	8.9	-32.6	93.3
	13.8	0.5	-7.6	70.3
10724/E05			6.3	25.8
10724/E06	8.3	1.6		46.8
10724/E07	-3.6	9.4	21.0	27.0
10724/E09	14.3	6.3		84.0
10724/E10	7.3	41.4	34.9	39.3
10724/E11	5.1	-26.8	5.0	73.0
10724/F02	9.7	27.4	0.8	13.0

208 Table 14 (continued)

10724/F03	-12.5	9.8	45.8	44.2
10724/F04	10.2	2.9		81.9
10724/F05	-7.2	-16.4	-52.1	
10724/F06	13.8	-3.5	-0.6	67.0
10724/F07	-6.0	8.9	-5.5	51.2
10724/F09	17.1		-6.2	47.3
10724/F10	2.7	-14 6		20.5
10724/F10	4.5	-10.4	1.5	55.6
10724/G02		3.8	-6.9	49.3
10724/G02	15.1	42.5	-7.6	44.9
10724/G03	-8.4 -7.9	7.8	-2.7	36.7
10724/G04		12.9	-12.4	71.0
	-0.1	-20.8	-10.3	61.0
10724/G06	0.1	3.2	-69	20.3
10724/G07	-1.9	-11.7	-41.6	2.3
10724/G09	9.1	-21.7	-18.0	-2.8
10724/G10	7.0	-10.6	-15.9	62.8
10724/G11	6.8	-29.5	-29.1	11.2
10725/A02	-2.0	3.9	-14.2	46.6
10725/A03	3.6	-38.2	5.9	68.0
10725/A04	-8.6	26.2	-3.2	55.3
10725/A05	-13.9	7.9	13 1	47.5
10725/A06	-7.3	-9.5	40 9	71.7
10725/A07	-12.3	18.2	179	59.3
10725/A08	-2.9	10.9	14 1	45.3
10725/A09	-13.9	4.9	29.4	44.3
10725/A10	-3.2	14.0	33.7	43.2
10725/A11	-21.9	14.6	18.9	49.1
10725/B02	-2.8	2.5	-7.5	66.9
10725/B03	4.9	-15.3	7.8	70.8
10725/B04	1.1	76.9	9.3	90.4
10725/B05	-61.0	20.4	44.7	68.3
10725/B06	-0.5		31.3	53.3
10725/B07	24.6	,,,,	100.8	74.0
10725/B08	-24.1	41.8	29.4	66.7
10725/B09	0.4	72.3	43.8	65.7
10725/B10	5.1	53.3	26.0	69.9
10725/B11	-42.3	43.0	66.3	76.3
10725/C02	7.0	-43.4	-5.1	6.3
10725/C03	2.0	-12.7	19.3	72.9
10725/C04	-27.3	31.8	25.1	75.9
10725/C05	-37.0	-21.9	28.9	31.7
10725/C06	-9.3	-11.5	46.6	54.7
10725/C07	65.0	-16.5	107.0	38.8
10725/C08	-8.7	-11.9	101.7	28.0
10725/C09	11.2	23.6	34.7	24.1
10725/C10	8.7	5.3	38.5	-0.6
10725/C11	104.5	-22.1	80.7	48.4
10725/D02	-3.6	-23.9	-8.4	14.0
10725/D03	-11.3	-2.5	5.4	72.9
10725/D04	3.6	4.3	12.2	55.1
10725/D05	2.3	-19.7	10.7	24.5
10725/D06	-0.5	-26.4	21.7	24.7
10725/D07	2.6	-25.8	18.4	37.0
10725/D08	1.8	20.0	38.5	39.2

Z09
Table 14
(continued)

10725/D10	10725/D09	-0.9	4.3	35.6	28.0
10725/F02					
10725/E02					
10725/E03					
10725/E04 -38.8 31.2 3.1 59.0 10725/E05 -0.2 -5.5 27.5 28.2 10725/E06 -1.8 -1.7 39.0 36.7 10725/E07 9.7 12.5 28.9 45.3 10725/E08 12.1 14.2 48.6 39.7 10725/E09 7.0 31.4 37.5 22.4 10725/E10 9.3 6.1 28.4 4.7 10725/E11 18.9 -36.0 20.8 9.6 10725/F02 5.8 -3.7 -15.1 27.8 10725/F03 4.3 -36.2 -27.1 63.2 10725/F03 4.3 -36.2 -27.1 63.2 10725/F04 6.9 49.6 4.6 38.1 10725/F05 -0.8 -18.9 -5.6 15.5 10725/F06 -1.0 -37.8 14.1 41.8 18.10725/F06 6.1.0 -37.8 14.1 41.8 10725/F09 6.9 16.4 15.0 67.8 10725/F09 6.8 32.2 28.4 48.5 10725/F09 6.8 32.2 28.4 32.7 32.7 32.7 10725/F09 6.8 32.2 32.7 32.7 32.7 32.7 32.7 32.7 32.7					
10725/E05					
10725/E06				}	
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10725/G11 -28.0 -32.4 22.2 25.7 10726/A03 -2.6 -12.5 4.3 70.1 10726/A04 7.6 40.8 44.2 85.7 10726/A05 -7.1 -28.4 22.1 75.2 10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 <td>10725/G09</td> <td>15.2</td> <td>6.5</td> <td>43.8</td> <td>4.7</td>	10725/G09	15.2	6.5	43.8	4.7
10725/G11 -28.0 -32.4 22.2 25.7 10726/A03 -2.6 -12.5 4.3 70.1 10726/A04 7.6 40.8 44.2 85.7 10726/A05 -7.1 -28.4 22.1 75.2 10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 <td>10725/G10</td> <td>11.1</td> <td>17.8</td> <td>44.7</td> <td>27 7</td>	10725/G10	11.1	17.8	44.7	27 7
10726/A03 -2.6 -12.5 4.3 70.1 10726/A04 7.6 40.8 44.2 85.7 10726/A05 -7.1 -28.4 22.1 75.2 10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09	10725/G11			22.2	25.7
10726/A05 -7.1 -28.4 22.1 75.2 10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11	10726/A03			4.3	70.1
10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03	10726/A04	7.6	40.8	44.2	85.7
10726/A06 -4.6 0.2 22.1 54.7 10726/A07 -72.3 88.7 -36.8 101.4 10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03	10726/A05				75.2
10726/A08 -4.0 -28.4 10.7 63.1 10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A06	-4.6	0.2	22.1	54 7
10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A07	-72.3	88.7	-36.8	101.4
10726/A09 -4.5 -6.3 16.4 70.8 10726/A10 3.7 26.5 8.1 58.9 10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A08	-4.0	-28.4	10.7	63.1
10726/A11 0.5 6.2 23.3 70.8 10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A09	-4.5		16.4	70.8
10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A10	3.7	26.5	8.1	58.9
10726/B03 11.1 3.5 16.4 81.1 10726/B04 16.8 71.1 39.1 78.9 10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/A11	0.5	6.2	23.3	70.8
10726/B05 13.2 49.0 27.1 96.8 10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B03	11.1		1	
10726/B06 11.3 6.6 34.1 76.1 10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B04	16.8	71.1	39.1	78.9
10726/B07 -36.5 72.4 -59.5 98.5 10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B05		49.0	27.1	
10726/B08 12.2 23.6 24.6 60.2 10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B06				
10726/B09 7.5 28.9 22.7 72.3 10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B07				
10726/B10 3.7 40.8 6.2 58.5 10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B08				
10726/B11 7.4 39.4 23.3 64.4 10726/C03 24.9 29.8 28.4 38.9	10726/B09			22.7	
10726/C03 24.9 29.8 28.4 38.9	10726/B10		40.8		
	10726/B11	7.4	39.4	23.3	
10726/C04 12.3 58.4 36.6 91.7	10726/C03		29.8	28.4	
10726/C05 4 0 16.7 25.2 58.0	10726/C05	4 0	16.7	25.2	58.0

Table 14 (continued)

10726/C06	23.8	-09	36.0	42.6
10726/C07	-17.0	40.8	-67.7	84.9
10726/C08	3.4	7.5	21.4	46.8
10726/C09	12.9	-14.3	26 5	48.5
10726/C10	5.5	2.8	16 4	36.7
10726/C11	-32.2	4.8	51.1	34.7
10726/D03	1 21.6	-5 4	21.4	52.1
10726/D04	7.8	-20.1	34.1	62.9
10726/D05	8.2	-8.1	20.4	51.2
10726/D06	16.3	-24.4	28.4	42.8
10726/D07	-26.9	18.5	-81.0	84.6
10726/D08	12.1	-11.4	22.1	39.5
10726/D09	14.4	-6.5	22.1	45.7
10726/D10	14.7	-6.5	32.2	35.3
10726/D11	10.5	-6.3	30.9	9.6
10726/E03	-5.5	-15.9	20.2	62.4
10726/E04	8.1	53 0	12.6	85.5
10726/E05	8.1	5.5	4.3	71.0
10726/E06	6.2	-20.6	41.7	-7.4
10726/E07	-40.0	20.5	-12.1	84.0
10726/E08	4.1	-8.5	34.1	58.9
10726/E09	9.9	10.0	34.7	50.3
10726/E10	16.5	-9.0	37.9	41.5
10726/E11	16.2	-14.1	30.3	34.5
10726/F03	8.3	-17.4	5.6	54.1
10726/F04	31,5	33.4	18.3	93.5
10726/F05	8.9	-26.8	-17.8	51.2
10726/F06	17.7	-24.1	17.0	16.2
10726/F07	9.6	76.2	-99.4	96.1
10726/F08	15.3	-21.5	28.4	67.3
10726/F09	9.6	-22.8	-2.6	66.8
10726/F10	7.0	-17.4	9.4	51.4
10726/F11	13.6	-16 8	25.2	57.6
10726/G03	11.3	-172	4.3	26.8
10726/G04	9.7	60.6	14.5	72.8
10726/G05	14.9	5.1	6.2	81.1
10726/G06	7.0	-37 5	-26.6	19.9
10726/G07	-13.7	54.4	-107.6	94.8
10726/G08	2.9	-2.7	14.5	39.1
10726/G09	3.6	3.3	13.2	42.4
10726/G10	10.5	6.0	-7.0	26.8
10726/G11	9.1	1.3	-7.7	11.8
10727/A02	-1.3	3.2	-10.3	52.0
10727/A03	6.3	-19.2	-4.5	40.7
10727/A04	-4.6	28.2	12.3	80.9
10727/A05	4.2	-3.0	5.7	29.0
10727/A06	-17.1	-6.3	13.7	32.7
10727/A07	-10.7	-3.7	12.3	61.1
10727/A08	-0.6	9.7	15.2	9.7
10727/A09	-16.8	12.7	16.6	44.2
10727/A10	-6.4	89.0	18.1	95.2
10727/A11	7.4	6.2	10.8	16.5
10727/B02	2.4	-18.4	-10.3	90.5
10727/B03	-13.4	-2.8	-7.4	84.5
				

Table 14 (continued)

10727/B04	46.0	47.4	21.0	87.1
10727/805	10.5	39.0	9.4	83.3
10727/B06	-3.9	40.7	64	91.0
10727/B07	8.4	46.5	0.6	83.5
10727/B08	4.0	47.4	14.4	90.7
10727/B09	6.7	31.7	18.1	81.9
	3.9	94.0	29.7	99.2
10727/B10				
10727/B11	16.8	6.9	15.9 -12.5	73.8
10727/C02	-2.0	-28.5		
10727/C03	-3.2	14.6	11.5	11.9
10727/C04	0.2	27.6	23.2	81.7
10727/C05	13.7	11.8	7.9	
10727/C06	5.2	5.6	12 3	45.2
10727/C07	15.9	8.4	13.0	36.7
10727/C08	4.9	3.6	23.2	47.8
10727/C09 i	-13.5	16.6	21 7	37.9
10727/C10	-35.3	85.3	45 7	94.4
10727/C11	-25.6	-15 6	22.4	14.5
10727/D02	3.2	22.6	5.7	51.6
10727/D03	3.1	39.4	-3.0	24.0
10727/D04	25.9	39.6	6.4	76.0
10727/D05	8.5	3.4	-0.1	39.9
10727/D06	13.1	8.6	10.8	24.4
10727/D07	19.7	10.5	-14.7	50.6
10727/D08	14.1	-0.5	5.0	8.5
10727/D09	8.2	15.1	7.2	17.9
10727/D10	11.4	86.2	9.4	79.9
10727/D11	10.5	-23.7	17.4	17.3
10727/E02	9.3	22.4	-67	28.0
10727/E03	11.1	35.5	5.7	28.8
10727/E04	46.1	82.1	-7 4	98.4
10727/E05	17.1	12.9	-7.4	12.1
10727/E06	14.2	-9.3	9.4	-2.2
10727/E07	20.1	7.1	10.1	45.2
10727/E08	14.2	25.6	23.9	27.0
10727/E09	9.3	15.1	15 9	28 4
10727/E10	9.7	85.1	5.0	96.6
10727/E11	37.3	-33.4	7.9	-5.4
10727/F02	15.9	-0.5	11.5	52.0
10727/F03	8.9	36.8	-3.7	22.0
10727/F04	15.3	17.9	-10.3	92.0
10727/F05	21.8	-9.1	-3.7	6.0
10727/F06	14.5	4.9	8.6	37.7
10727/F07	21.4	-8.9	2.1	17.9
10727/F08	12.5	-5.4	10.1	36.9
10727/F09	-45.2	-2.0	21.7	9.3
10727/F10	15.9	74.1	9.4	93.4
10727/F11	17.3	-2.6	18.1	-3.0
10727/G02	7.1	37.5	-20.5	81.5
10727/G03	-3.5	19.4	-10.3	40.5
10727/G04	27.2	80.6	-27.0	94.0
10727/G05	8.0	11.2	-2.3	7.1
10727/G06	2.9	-12.1	-12.5	31.1
10727/G07	7.2	5.4	-24.1	29.6

212 Table 14 (continued)

10727/G08	15.7	10.0	7.	24.2
10727/G09	15.7	-19.6	-7.4	21.8
10727/G10	-5.6	-9.7	10.8	18.8
10727/G10		85.1	10.8	99.2
10728/A02	6.9	-3.5	15.9	-0.8
10728/A03		9.2	-7.9	25.6
10728/A04	-1.3	-25.8	-7.9	29.2
10728/A05	-3.5	28.0	15.6	28.5
10728/A05	-10.8 -10.4	17.7	4.5	31.8
10728/A07		17.2		19.7
10728/A08	-21.6	59.6	31.1	28.5
10728/A09	-1.4	24.1	0.5	40.2
10728/A10	-5.5 -16.3	19.3	10.3	53.1
10728/A11		-3.4	1.8	77.2
	-2.3	-0.6	-9.3	58.8
10728/802	-11.1	-10.5	-0.4	61.2
10728/803	-1.3	-36.6	10.3	74.4
10728/B04	-6.0	-2.0	9.8	67.2
10728/B05	-12.3	26.9	9.4	60 4
10728/806	4.7	38.1	7.6	56 0
10728/B07	31.4	11.1	20.9	82.2
10728/B08	14.8	34.7	-6.6	77.0
10728/B09	1.7	31.7	-0.4	81.7
10728/B10	3.9	16.8	2.7	79.3
10728/B11	-1.0	48.2	-12.4	80.3
10728/C02	-32.1	-35.4	42.3	15.5
10728/C03	10.5	9.7	24.9	16.9
10728/C04	-0.0	16.1	27.2	33.6
10728/C05	-21.7	16.1	23.2	33.7
10728/C06	8.4	4.2	2.7	22.9
10728/C07	-7.2	8.3	8.9	46.3
10728/C08	-2.2	17.5	9.4	25.5
10728/C09	14.5	-6.8	8.1	31.6
10728/C10	6.1	4.4	11.2	28.7
10728/C11	-10.1	21.8	8.5	45.2
10728/D02	-0.3	9.9	9.8	21.4
10728/D03	10.2	10.8	32.0	13.5
10728/D04	6.8	-11	26.7	23.1
10728/D05	4.9	12.7	7.2	29.5
10728/D06	10.4	5.8	5.8	23.2
10728/D07	8.1	2.4	2.3	21.8
10728/D08	13.5	6.9	2.7	34.7
10728/D09	10.5	-2 9	-3.9	27.6
10728/D10	17.9	18.6	-3.9	30.5
10728/D11	15.9	22.1	-10.2	52.5
10728/E02	5.4	7.4	15.2	5.4
10728/E03	13.2	9.5	12.0	11.9
10728/E04	5.5	10.1	23.2	25.6
10728/E05	17.4	7.4	5.8	53.4
10728/E06	6.6	-47	12.0	26.4
10728/E07	9.6	21.8	28.0	79.8
10728/E08	15.2	5.1	29.4	46.3
10728/E09	9.0	0.1	22.3	40.0
10728/E10	24.7	-20.8	13.8	57.2
10728/E11	16.3	-5.9	8.9	53.1

213
Table 14
(continued)

10728/F03	10728/F02	2.9	4.4	7 2	25.6
10728/F04					
10728/F05	·				
10728/F06				 	
10728/F07					
10728/F08					
10728/F09					
10728/F10					
10728/F11					
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10729/B10 -0.7 68.3 -13.9 32.6 10729/B11 7.8 18.8 4.2 36.6 10729/C02 6.0 16.9 9.1 18.2 10729/C03 11.0 25.7 13.7 13.5 10729/C04 -2.5 35.9 4.2 20.7 10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/B11 7.8 18.8 4.2 36.6 10729/C02 6.0 16.9 9.1 18.2 10729/C03 11.0 25.7 13.7 13.5 10729/C04 -2.5 35.9 4.2 20.7 10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C02 6.0 16.9 9.1 18.2 10729/C03 11.0 25.7 13.7 13.5 10729/C04 -2.5 35.9 4.2 20.7 10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C03 11.0 25.7 13.7 13.5 10729/C04 -2.5 35.9 4.2 20.7 10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C04 -2.5 35.9 4.2 20.7 10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C05 5.8 21.8 -5.6 15.5 10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C06 3.8 38.2 3.1 15.2 10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C07 -22.4 60.8 -1.8 58.4 10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C08 -20.3 25.4 -13.6 55.7 10729/C09 -26.4 33.2 -34.8 60.4					
10729/C09 -26.4 33.2 -34.8 60.4					
10720/040					
	10729/C10	2.5	45.7	3.5	15.8
10729/C11 10.4 35.9 -17.4 41.3					
10729/D02 12.2 5.7 15.6 31.7	10729/D02	12.2	5.7	15.6	
10729/D03 15.3 15.5 14.1 22.6		15.3	15.5	14.1	
10729/D04 -5.7 18.8 -12.8 33.1	10729/D04	-5.7			
10729/D05 2.2 22.1 2.3 28.1	10729/D05	2.2	22.1	2.3	28.1

214
Table 14
(continued)

10729/D06	0.2	45.7	1 2.7	30.2
10729/D07	-15.3	21,4	-20.0	25.5
10729/D08	-26.2	10.3	-21.1	27.6
10729/D09	-9.6	22.1	-12.1	34.8
10729/D10	4.1	11.3	-113	36.1
10729/D11	-2.0	19.2	0.1	18.8
10729/E02	26.6	8.0	28.4	11.7
10729/E03	6.9	20.1	29.2	27.5
10729/E04	9.7	19.5	26.5	9.8
10729/E05	46.8	12.6	29.9	13.4
10729/E06	12.1	43.7	24.7	-0.7
10729/E07	4.1	26.7	29.6	21.6
10729/E08	10.9	40.1	11.0	73.7
10729/E09	6.9	29.6	-11.7	85.0
10729/E10	5.7	50.3	11.8	7.5
10729/E11	70.9	25.7	22.4	50.8
10729/F02	18.9	-14.0	20.1	19.5
10729/F03	30.0	10.6	33.7	27.8
10729/F04	16.0	13.3	25.4	44.9
10729/F05	15.4	-4.8	31.5	33.8
10729/F06	36.4	15.9	29.6	44.3
10729/F07	-5.8	6.7	6.1	37.3
10729/F08	-3,4	10.3	0.8	44.6
10729/F09	-2.6	13.3	8.8	38.2
10729/F10	20.0	58.5	15.2	39.0
10729/F11	-1.5	25.4	7.2	15.2
10729/G02	18.8	-4.8	16.7	31.3
10729/G03	10.4	14.6	13.7	20.1
10729/G04	12.2	52.9	1,6	18.2
10729/G05	8.7	4.4	9.9	22.6
10729/G06	10.9	15.2	11.8	26.0
10729/G07	-2.5	-0.8	14.4	38.2
10729/G08	-1.0	6.0	0.8	39.9
10729/G09	-3.3	20.8	1.9	49.6
10729/G10	-9.1	60.1	-13.2	26.7
10729/G11	-0.5	23.4	3.8	15.4
10730/A02	-3.7	27.5	-23.1	39.5
10730/A03	-3.2	34.4	-11.2	62.3
10730/A04	-9.9	37.2	-5.1	70.6
10730/A05	-10.8	18.6	2.8	42.7
10730/A06	-7.0	6.7	6.3	61.0
10730/A07	-18.9	10.4	-23.9	55.4
10730/A08	-2.9	10.4	-6.0	69.0
10730/A09	1.9	1.1	-4.7	69.5
10730/A10	0.5	56.1	1.0	68.7
10730/A11	6.8	56.4	-6.4	91.0
10730/B02	5.0	10.4	5.4	66.3
10730/B03	-0.5	46.8	17.3	78.3
10730/B04	12.8	36.5	7.2	73.2
10730/B05	-0.5	8.5	-2.9	71.1
10730/B06	2.4	25.0	7.6	71.3
10730/B07	0.6	57.1	2.4	63.1
10730/B08	4.4	48.4	0.2	91.8
10730/B09	9.4	14.2	15.1	70.6
				

215 Table 14 (continued)

10730/B10	15.2	15.8	19.0	69.5
10730/B11	1.9	70.2	-13.9	81.7
10730/C02	48.8	2.7	26.5	31.2
10730/C03	25.5	-12.1	36.5	43.2
10730/C04	46.1	0.1	15.5	43.2
10730/C05		-9.8	8.5	46.1
10730/C06	5.3	8.5	7.6	34.7
10730/C07	7.3	20.3	1.0	37.4
10730/C08	-2.3	24.3	8.5	56.5
10730/C09	14.0	28.2	18.1	42.9
10730/C10	15.4	20.5	44.4	40.3
10730/C11	-8.0	38.4	16.4	66.6
10730/D02	12.4	18.6	24.3	34.7
10730/D03	8.4	9.9	19.0	34.2
10730/D03	9.1	10.4	20.8	33.6
10730/D05	11.9	12.6	-1.6	38.1
10730/D05	5.8	35.3		
10730/D03	8.8	43.0	-2.0 5.0	55.9
10730/D07	8.6	44.9	12.9	52.5 -13.6
10730/D08	9.8	44.9		
10730/D09			-1.6	59.1
10730/D10	-15.3 7.7	16.7 2.0	-3.3	18.5
			-0.7	9.7
10730/E02	24.8	17.7	16.4	18.8
10730/E03	34.5	65.3	14.6	53.3
10730/E04	22.1	13.5	18.6	35.2
10730/E05	8.7	15.8	28.7	49.0
10730/E06	11.1	1.5	26.0	52.8
10730/E07	12.0	18.8	30.0	37.1
10730/E08	25.1	6.2	48.4	40.3
10730/E09	21.8	21.7	20.3	33.9
10730/E10	26.0	9.3	39.6	63.6
10730/E11	29.1	19.1	31.7	77.2
10730/F02	18.4	2.9	20.3	-6.2
10730/F03	11.7	10.4	1.5	-0.6
10730/F04	18.3	-4.8	28.7	36.0
10730/F05	19.6	-16.3	19.5	23.5
10730/F06	21.9	-0.6	3.2	56.5
10730/F07	67.5	27.3	-2.0	60.7
10730/F08	2.1	0.8	-0.3	46.4
10730/F09	14.4	17.9	13.3	71.1
10730/F10	13.4	6.2	1.9	42.1
10730/F11	-1.3	-24.1	4.5	53.6
10730/G02	23.3	20.8	18.1	41.1
10730/G03	15.2	-6.9	44.0	43.2
10730/G04	7.4	-6 .7	21.6	47.7
10730/G05	22.3	-18.2	65.0	35.8
10730/G06	8.2	-2.7	0.2	17.7
10730/G07	8.3	6.4	19.9	26.2
10730/G08	23.3	9.5	20.3	16.6
10730/G09	18.7	-20.3	23.0	16.4
10730/G10	11.3	3.1	22.1	42.1
10730/G11	-1.4	26.2	-0.3	46.1
10731/A02	2.7	14.8	-3.9	23.9
10731/A03	2.5	10.8	7.5	54.8
	<u> </u>			

Table 14 (continued)

10731/A04	5.0	20.2	5.1	43.6
10731/A05	-6.5	34.3	14.1	85.8
10731/A06	-5.5	30.1	1.3	53.0
10731/A07	-4.3	39.4	4.6	49.5
10731/A08	-13.8	25.7	-2.5	59.9
10731/A09	-2.7	21.9	-14.4	46.7
10731/A10	-5.3	26.3	-3.5	41.2
10731/A11	3.1	16.1	-0.1	53.4
10731/B02	6.5	15.5	13.2	71.6
10731/B03	1.9	12.3	9.9	60.9
10731/804	12.0	31.3	0.3	71.0
10731/B05	3.8	35.9	17.9	86.0
10731/B06	6.2	37.5	5.6	56.2
10731/807	11.7	29.1	6.0	41.6
10731/B08	6.2	37.2	-23.4	57.4
10731/B09	-0.5	15.0	0.3	29.6
10731/B10	1.3	50.5	4.6	72.9
10731/B11	6.9	55.2	-13.0	58.2
	3.1	-6.9	-2.5	11.1
10731/C03	4.5	9.1	11.3	38.7
10731/C04	10.5	31.0	15.1	32.5
10731/C05	14.9	35.5	22.7	78.3
10731/C06	13.8	23.1	7.0	18.2
10731/C07	70.4	35.5	31.3	-11,6
10731/C08	10.2	23.6	-3.0	25.8
10731/C09	15.1	16.8	-6.3	22.7
10731/C10	19.7	20.9	6.5	23.3
10731/C11	5.5	29.6	-9.2	16.2
10731/D02	-8.4	4.9	17.9	8.7
10731/D03	17.3	16.3	28.4	40.2
10731/D04	9.3	15.8	6.5	24.5
10731/D05	32.7	53.9	46.0	92.7
10731/D06	16.1	23.2	8.0	59.7
10731/D07	12,3	25.9	2.7	45.9
10731/D08	25.8	16.8	-8.7	44.2
10731/D09	6.1	12.6	-2.0	23.9
10731/D10	13.0	15.8	9.9	21.1
10731/D11	15.2	43.6	8.4	56.6
10731/E02	11.2	7.9	13.7	49.1
10731/E03	-1.4	10.4	15.6	20.7
10731/E04	23.8	13.6	30.8	55.6
10731/E05	7.0	17.7	27.0	82.2
10731/E06	2.6	10.4	-12.0	37.7
10731/E07	12.6	38.4	3.7	45.9
10731/E08	10.5	40.1	8.9	59.0
10731/E09	52.5	17.2	23.2	27.0
10731/E10	33.1	25.1	21.7	35.5
10731/E11	17.9	26.4	27.9	60.7
10731/F02	11.1	17.7	14.1	47.5
10731/F03	7.9	8.4	11.8	40.6
10731/F04	24.5	5.0	3.2	17.0
10731/F05	17.6	19.5	20.3	84.4
10731/F06	2.2	7.2	-23.4	20.9
10731/F07	13.3	37.7	1.3	34.7

Table 14 (continued)

10721/509	0.2	7 1	14	22.5
10731/F08 10731/F09	9.2	7.1 -0.7	4.1	23.5
		7.9	15.6	
			28.4	48.1
		42.3	20.3	60.1
10731/G02	16.8	4.7	-10.1	15.2
10731/G03	12.9	7.7	6.5	33.7
10731/G04		7.1	0.3	23.3
10731/G05	17.5	18.5	8.0	72.4
10731/G06		2.3	-0.6	33.3
10731/G07	31.6	0.7	40.8	10.9
10731/G08	18.2	13.3	-13.9	19.5
10731/G09	13.3	8.9	-8.7	4.4
10731/G10	-9.0	5.5	5.6	10.3
10731/G11	1.5	67.2	16.0	64.3
10732/A02	-12.5	5.1	10.8	53.7
10732/A03	-9.9	0.8	-3.8	37.4
10732/A04	-14.1	-10.6	-9.4	34.8
10732/A05	-3.9	4.6	-12.9	20.5
10732/A06	-0.0	-1.4	12.3	5.7
10732/A07	-19.8	-0.3	0.7	26.1
10732/A08	-10.0	12.1	31.0	32.7
10732/A09	-11.2	39.7	8.8	60.3
10732/A10	10.2	6.1	7.3	20.3
10732/A11	-0.6	1.8	40.1	65.3
10732/B02	2.9	-26.0	23.5	78.0
10732/B03	8.2	-15.3	17.4	58.1
10732/B04	-1.3	-22.1	16.9	79.5
10732/B05	2.8	17.0	21.9	71.2
10732/B06	8.1	12.8	-12.4	74.3
10732/B07	1.6	15.8	21.4	75.1
10732/B08	8.0	7.8	16.9	64.4
10732/B09	14.0	2.0	18.4	69.2
10732/B10	12.1	0.6	0.7	51.5
10732/B10	9.0	9.3	70.9	73.7
10732/C02	11.9	-6.5	7.3	40.1
10732/C02	14.7	1.4	7.3	14.0
			3.8	30.6
10732/C04	12.8	-14.7	-17.0	18.5
10732/C05	11.2	-22.8	5.3	21.6
10732/C06 10732/C07	11.8	-43.2 -28.6	4.3	26.5
10732/C07	15.4 7.6	-28,6 1.6	17.9	54.5
			15.4	37.9
10732/C09	8.0	-3.9	5.8	43.0
10732/C10	15.1	1.2		
10732/C11	18.2	-5.0	16.4	31.9
10732/D02	9.2	8.7	-24.0	50.2
10732/D03	22.5	-18.7	26.0	24.9
10732/D04	24.6	-11.4	50.7	40.7
10732/D05	15.7	-36.7	4.3	30.2
10732/D06	16.3	3.6	16.4	24.3
10732/D07	14.7	-19.1	-3.8	43.2
10732/D08	33.3	-20.6	30.5	49.4
10732/D09	15.2	-9.9	15.9	40.3
10732/D10	25.5	-16.6	24.5	33.1
10732/D11	18.8	-13.4	18.9	48.6

218
Table 14
(continued)

10732/E02	13.1	0.8	4.8	33.3
10732/E03	16.7	-1.6	48.7	3.9
10732/E04	15.8	-10.6	29.5	8.2
10732/E05	18.7	-17.0	41.1	2.2
10732/E06	2.8	-11.0	16.9	-2.1
10732/E07	21.3	-8.5	42.2	15.2
10732/E08	13.6	-21.7	32.6	29.4
10732/E09	15.3	-7.2	46.7	18.1
10732/E10	16.7	-3.3	35.6	1.6
10732/E11	16.2	-32.2	47.7	41.4
10732/F02	7.0	23.1	-9.4	55.6
10732/F03	31.9	54.1	51.8	68.6
10732/F04	16.2	-0.1	23.5	57.2
10732/F05	37.3	-30.7	12.8	58.9
10732/F06	11.6	-8.0	0.2	45.7
10732/F07	31.0	-12.5	38.6	65.5
10732/F08	12.6	-11.9	14.9	76.6
10732/F09	25.6	-13.4	25.5	79.7
10732/F10	14.1	0.8	15 9	65.1
10732/F11	21.9	-21.5	77.5	75.2
10732/G02	8.1	-0.7	10.3	39.5
10732/G03	0.8	-20.0	36.1	38.1
10732/G04	12.6	8.0	25.0	24.9
10732/G05	17.2	3.8	15.4	15.2
10732/G06	26.5	-12.1	0.2	16.2
10732/G07	4.6	-21.9	21.4	23.9
10732/G08	10.0	-20.4	37.6	44.7
10732/G09	16.9	-34.8	9.8	33.9
10732/G10	14.0	-38.2	20.4	45.7
10732/G11	10.9	-33.7	38.6	63.0
10733/A02	-5.2	25.9	11.5	74.6
10733/A03	45.0	33.6	23.2	24.9
10733/A04	-11.2	32.8	-14.1	24.0
10733/A05	-23.3	55.2	-4.0	18.2
10733/A06	-16.6	45.1	-24.3	33.7
10733/A07	-27.4	28.5	-12.9	27.2
10733/A08	-17.1	19.5	-10.1	27.2
10733/A09	-11.9	25.9	-7.6	22.1
10733/A09	-9.3	14.2	-13.3	21.1
10733/A11	15.0	23.0	4.2	43.5
10733/B02	-7.4	31.6	14.7	74.6
10733/B03	3.1	14.4	35.8	62.2
10733/B04	-3.3	28.5	24.9	56.3
10733/B05	-1.1	26.7	27.3	61.3
10733/B06	4.6	43.6	-9.2	71.4
10733/B07	1.2	32.7	4.2	73.5
10733/B08	-16.0	32.5	-15.7	65.5
10733/B09	-2.6	21.1	7.0	64.5
10733/B10	5.7	11.8	-59.6	65.1
10733/B11	22.5	12.5	23.7	36.6
10733/C02	5.8	31.6	15.1	71.8
10733/C03	17.0	14.4	28.1	29.3
10733/C03	8.4	29.0	19.2	18.4
10733/C05	11.5	17.2	11.1	23.2
107337003	11.5	11.2	11.1	29.2

219
Table 14
(continued)

10733/C06	4.7	22.7	20.0	4.1
10733/C07	1.2	16.7	4.6	10.2
10733/C08	-28.5	65.8	-3.6	85.7
10733/C09	-18.0	46.0	91.9	16.3
10733/C10	-7.6	36.0	-6.4	20.5
10733/C11	42.8	15.8	62.2	35.1
10733/D02	3.1	12.5	17.6	63.4
10733/D03	33.2	11.2	40.7	32.8
10733/D04	15.5	19.9	26.5	37.7
10733/D05	16.5	10.6	16.8	25.1
10733/D06	17.9	30.8	1.3	-19.4
10733/D07	-1.4	37.4	0.9	-6.8
10733/D08	-8.3	38.3	42.3	80.0
10733/D09	9.8	48.3	33.8	38.7
10733/D10	2.9	46.8	-10.1	22.8
10733/D11	1.0	33.7	4.0	31.6
10733/E02	0.8	-1.3	20.8	60.5
10733/E03	42.6	10.7	43.1	26.8
10733/E03	2.1	45.4	-13.7	17.5
10733/E05	10.6	58.3	-33.2	2.9
10733/E05	13.5	37.3	22.4	10.4
10733/E07	13.2	19.9	29.3	-10.1
10733/E08				81.1
10733/E09	-5.1 13.4	54.2 72.4	75.2 35.8	62.6
10733/E10		31.3		52.8
	5.5		10.3	
10733/E11	5.5	31.6	15.9	71.8
10733/F02	-15.7	11.3	3.8	71.6
10733/F03	17.5	-3.6	24.5	24.2
10733/F04	21.4	76 3	-28.7	65.1
10733/F05	26.2	84.6	-25.1	65.1
10733/F06	19.3	17.8	-4.8	20.9
10733/F07	16.4	19.2	1.7	-16.4
10733/F08	-13.2	17.2	-32.4	66.6
10733/F09	-2.1	30.1	-0.3	52.8
10733/F10	8.5	21.9	-5.6	24.4
10733/F11	4.1	0.6	-17.8	44.4
10733/G02	8.3	-6.2	-76	64.5
10733/G03	24.7	0.7	12.7	30.5
10733/G04	11.5	10.6	11.9	20.3
10733/G05	19.2	1.5	-1.1	1.8
10733/G06	37.0	5.2	0.1	0.8
10733/G07	19.5	18.1	-6.8	8.5
10733/G08	2.5	44.2	68.7	79.0
10733/G09	77.8	38.7	-17.0	41.4
10733/G10	12.7	18.2	-58.0	41.9
10733/G11	3.3	-1.0	-4.4	32.6
10734/A02	4.1	0.0	-3.8	51.1
10734/A03	10.1	18.5	22.3	87.8
10734/A04	0.6	11.4	11.7	68.0
10734/A05	9.1	22.6	2.9	69.9
10734/A05	-6.4	-6.4	-9.9	46.9
10734/A07	-9.4	15.2	21.9	89.3
10734/A08	0.1	6.8	9.1	71.5
10734/A09	-7.9	27.3	9.5	88.4
101071003	1 -1.3	1 21.5	1 .3.5	

219/1 Table 14 (continued)

10734/A10	4.4	27.8	26.3	55.4
10734/A11	6.3	12.5		51.9
10734/B02	8.5	-8.9	-2.9	61.9
10734/B03	21.7	45.1	13.0	90.1
10734/B04	2.8	38.7	14.4	88.4
10734/B05	-2.3	17.8	56.3	67.8
10734/B06	-0.9	54.0	0.2	91.2
10734/B07	9.1	65.5	18.8	93.2
10734/B08	-0.5	19.3	-2.4	56.1
10734/B09	-32.3	34.9	12.6	94.3
10734/B10	15.7	60.7	7.7	82.6
10734/B11	12.6	50.9	-5.5	83.6
10734/C02	-3.9	-6.7	36.0	78.6
10734/C03	-5.6	48.6	24.5	88.2
10734/C04	-37.6	38.1	24.5	90.7
10734/C05	-10.3	9.3	3.8	52.7
10734/C06	-1.7	18.4	-0.2	48.3
10734/C07	-2.7	41.0	32.0	96.8
10734/C08	-34.2	35.1	5.5	93.2
10734/C09	-13.3	36.2	11.3	88.6
10734/C10	10.1	24.4	17.4	11.6
10734/C11	6.3	18.0	9.1	23.9
10734/D02	-11.5	5.2	6.4	46.0
10734/D03	17.4	19.6	24.1	78.6
10734/D04	6.1	-10.7	13.5	46.9
10734/D05	2.4	-9.6	8.2	55.0
10734/D06	0.0	1.3	-9.1	30.6
10734/D07	14.7	51.1	28.1	92.0
10734/D08	2.5	-13.7	2.0	49.8
10734/D09	-11.6	21.0	42.2	88.0
10734/D10	11.1	-4.4	9.9	20.6
10734/D11	9.8	14.6	17.0	33.9
10734/E02	7.9	-10.8	50.1	66.9
10734/E03	26.9	55.0	27.2	99.3
10734/E04	10.7	-7.8	26.7	88.9
10734/E05	10.6	7.9	17.9	63.6
10734/E06	28.4	6.3	13.5	50.6
10734/E07	27.9	82.4	8.2	100.8
10734/E08	26.6	24.2	13.0	89.1
10734/E09	8.0	73.0	1.1	96.2
10734/E10	18.5	-5.0	29.8	27.9
10734/E11	19.2	-8.0	16.1	67.1
10734/F02	6.2	0.7	10.4	55.0
10734/F03	4.2	24.8	-24.1	86.8
10734/F04	-2.6	3.9	25.0	76.5
10734/F05	9.8	-15.6	-1.1	73.8
10734/F06	11.0	-17.1	-21.4	64.2
10734/F07	6.6	33.7	-5.1	95.7
10734/F08	4.8	-23.6	-6.0	66.3
10734/F09	-3.7	3.1	-17.4	93.9
10734/F10	14.8	-8.3	25.8	44.8
10734/F11	13.3	-15.6	16.1	47.3
10734/G02	1.5	3.4	14.8	63.6
10734/G03	18.7	82.8	-3.8	93.4

219/2 Table 14

Table 14 (continued)

10734/G04	-1.1	62.9	16.1	72.1
10734/G05	7.4	-0.3	2.9	57.7
10734/G06	16.5	12.5	-18.8	43.1
10734/G07	21.9	51.1	-25.0	96.6
10734/G08	11.6	33.7	0.2	82.2
10734/G09	8.5	21.4	-7.7	84.7
10734/G10	10.8	3.8	9.9	19.3
10734/G11	8.7	4.1	-25.4	20.2

220

Claims:

1. A combinatorial library of indolinone compounds, comprising at least ten indolinones that can be formed by reacting oxindoles with aldehydes.

- 2. The combinatorial library of claim 1 wherein said oxindoles are type A oxindoles.
- 3. The combinatorial library of claim 1 wherein 10 said aldehydes are type B aldehydes.
 - 4. A method of making an indolinone comprising the steps of
- (a) creating a combinatorial library of indolinones 15 by reacting a series of oxindoles with a series of aldehydes,
 - (b) testing said indolinones in biological assays,
 - (c) selecting one or more indolinones with favorable activity; and
- 20 (d) synthesizing one or more of said indolinones selected in step (c).
- 5. A 3-[(indole-3-yl)methylene]-2-indolinone compound having a substituent at the 1' position of the indole, where the substituent at the 1' position is selected from the group consisting of,
- (a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally
 30 substituted with one or more halogen, aldehyde, or trihalomethyl substituents;
 - (b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is

optionally substituted with one or more halogen or trihalomethyl substituents;

- (c) an aldehyde or ketone of formula $-CO-R_{12}$, where R_{12} is selected from the group consisting of hydrogen, 5 alkyl, and a five or six membered heterocyclic ring;
- (d) a carboxylic acid of formula $-(R_{13})\,n$ -COOH or ester of formula $-(R_{14})\,m$ -COO- R_{15} , where R_{13} , R_{14} , and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (e) a sulfone of formula $-(SO2)-R_{16}$, where R_{16} is selected from the group consisting of alkyl and a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;
- (f) $-(R^{17})_n$ -(indole-1-yl) or $-(R)_m$ -CHOH-(R)p-(indole-1-yl), where the indol moiety is optionally substituted with an aldehyde and R_{17} , R_{18} , and R_{19} are alkyl and m, n, and p are independently 0 or 1; and
- (g) taken together with a 2' substituent of the 20 indole ring forms a tricyclic moiety, where each ring in the tricyclic moiety is a five or six membered heterocyclic ring.
- The compound, salt, isomer, metabolite, ester,
 amide, or prodrug of claim 5, wherein said compound has the formula,

$$R_{4}$$
 R_{5}
 R_{7}
 R_{1}
 R_{2}
 R_{2}
 R_{3}
 R_{4}
 R_{5}
 R_{7}
 R_{1}
 R_{2}
 R_{3}
 R_{4}
 R_{5}
 R_{5}
 R_{6}
 R_{7}
 R_{1}
 R_{1}
 R_{2}
 R_{3}
 R_{4}

where (a) R_1 is selected from the group consisting of,

- (i) alkyl that is optionally substituted with 5 a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered 10 monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- (iii) an aldehyde or ketone of formula $-\text{CO-R}_{12}$, where R_{11} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
 - (iv) a carboxylic acid of formula -(R $_{13}$) $_n$ -COOH or ester of formula -(R $_{14}$) m-COO-R $_{15}$, where R $_{13}$, R $_{14}$, and R $_{15}$

and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;

- (v) a sulfone of formula $-(SO_2)-R_{16}$, where R_{16} is selected from the group consisting of alkyl or a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;
- $(vi) (R_{17})_n (indole-1-yl) \text{ or } (R_{18})m CHOH (R_{19})p (indole-1-yl), where the indol moiety is optionally 0 substituted with an aldehyde and <math>R_{17}$, R_{18} , and R_{19} are alkyl and n, m, and p are independently 0 or 1;
- (vii) taken together with a 2' substituent of the indole ring forms a tricyclic moiety, where each ring in the tricyclic moiety is a five or six membered heterocyclic ring;
 - (b) R_2 , R_3 , R_4 , R_5 , and R_6 are selected from the group consisting of,
- (i) hydrogen or alkyl that is optionally substituted with a monocyclic or bicyclic five, six,
 20 eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring 25 is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (iii) an aldehyde or ketone of formula $-\text{CO-R}_{20}$, where R_{20} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- 30 (iv) a carboxylic acid of formula $-(R_{21})\,n$ -COOH or ester of formula $-(R_{22})\,-$ COO $-R_{23}$, where R_{21} , R_{22} , and R_{23} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

- (v) halogen or an alcohol of formula (R24)m-OH or an ether of formula $-(R_{24})_0-O-R_{25}$, where R_{24} and R25 are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (vi) $-NR_{26}R_{27}$, where R_{26} and R_{27} are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring; or $-NHCOR_{28}$, where R_{28} is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (vii) $-SO2NR_{29}R_{30}$, where R_{29} and R_{30} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
 - (viii) any two of R_3 , R_4 , R_5 , or R_6 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;
 - (c) $R_{\text{1}},\ R_{\text{8}},\ R_{\text{9}},\ \text{and}\ R_{\text{10}}$ are independently selected from the group consisting of,
- (i) hydrogen or alkyl that is optionally substituted with a monocyclic or bicyclic five, six,
 25 eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, aldehyde, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring 30 is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (iii) an aldehyde or ketone of formula $-CO-R_{31}$, where R_{31} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

- (iv) a carboxylic acid of formula $-(R_{32})\,n$ -COOH or ester of formula $-(R_{33})\,m$ -COO- R_{34} , where R_{32} , R_{33} , and R_{34} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and 5 n and m are independently 0 or 1;
 - (v) halogen or an alcohol of formula (R_{35}) m-OH or an ether of formula $-(R_{35})$ n-O- R_{36} , where R_{35} and R_{36} are independently chosen from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

10

30

- (vi) -NR₃₇R₃₈, where R₃₇ and R₃₈ are independently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring; or -NHCOR₃₉, where R₃₉ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (vii) $-SO2NR_{40}R_{41}$, where R_{40} and R_{41} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (viii) any two of R_7 , R_8 , R_9 , or R_{10} taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and
 - (d) R_{11} is hydrogen or alkyl; provided that at least one of R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , or R_{10} is alkyl or provided that at least four of R_1 , R_2 , R_3 , R_4 , R_5 , or R_6 are not hydrogen.

7. An optionally substituted 3-[(tetrahydroindole-2-yl)methylene]-2-indolinone or 3-[(cyclopentano-b-pyrrol-2-yl)methylene]-2-indolinone compound.

8. The indolinone compound of claim 7 of formula XIX or XX,

XIX

$$\begin{array}{c|c}
R_{2} & R_{3} & R_{3} \\
R_{3} & R_{3} & R_{4} \\
R_{4} & R_{5} & R_{5} \\
R_{5} & R_{5} & R_{5} \\
R_{7} & R_{7} & R_{7} \\
R_{8} & R_{1} & R_{2} \\
R_{1} & R_{2} & R_{3} \\
R_{1} & R_{2} & R_{3} \\
R_{2} & R_{3} & R_{4} \\
R_{3} & R_{4} & R_{5} \\
R_{4} & R_{5} & R_{5} \\
R_{5} & R_{5} & R_{5} \\
R_{7} & R_{7} & R_{7} & R_{7} \\
R_{1} & R_{2} & R_{3} & R_{5} \\
R_{2} & R_{3} & R_{3} & R_{5} \\
R_{3} & R_{4} & R_{5} & R_{5} \\
R_{4} & R_{5} & R_{5} & R_{5} \\
R_{5} & R_{5} & R_{5} & R_{5} \\
R_{5} & R_{5} & R_{5} & R_{5} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{7} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{8} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{8} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{8} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{8} & R_{7} & R_{7} & R_{7} & R_{7} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9} \\
R_{9} & R_{9} & R_{9} & R_{9} & R_{9$$

5

XX

$$R_{3}$$
 R_{4}
 R_{5}
 R_{4}
 R_{5}
 R_{4}
 R_{5}
 R_{5}
 R_{7}
 R_{1}
 R_{2}
 R_{3}
 R_{4}
 R_{5}
 R_{5}
 R_{5}
 R_{5}
 R_{5}

or a pharmaceutically acceptable salt, isomer, metabolite, 10 ester, amide, or prodrug thereof

- where (a) R_1 is selected from the group consisting of,
- (i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten
 5 membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered
 monocyclic or bicyclic heterocyclic ring, where the ring
 10 is optionally substituted with one or more halogen or
 trihalomethyl substituents;
 - (iii) ketone of formula $-CO-R_{12}$, where R_{11} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- 15 (iv) a carboxylic acid of formula $-(R_{13})_n$ -COOH or ester of formula $-(R_{14})_m$ -COO- R_{15} , where R_{13} , R_{14} , and R_{15} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and n and m are independently 0 or 1;
- (v) a sulfone of formula $-(SO_2)-R_{16}$, where R_{16} is selected from the group consisting of alkyl or a five or six membered heterocyclic ring, where the ring is optionally substituted with an alkyl moiety;
- $(vi) (R_{17})_n (indole-1-yl) \text{ or } (R_{18})_m CHOH (R_{19})p-25$ (indole-1-yl), where the indolemoiety is optionally substituted with an aldehyde and R_{17} , R_{18} , and R_{19} are alkyl and n, m, and p are independently 0 or 1;
- (vii) taken together with a 2' substituent of
 the indole ring forms a tricyclic moiety, where each ring
 30 in the tricyclic moiety is a five or six membered heterocyclic ring;
 - (b) R_2 , R_3 , R_3 ', R_4 , R_4 ', R_5 , R_5 ', R_6 , and R_6 ' are selected from the group consisting of,
 - (i) hydrogen;

- (ii) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- 10 (iv) ketone of formula $-CO-R_{20}$, where R_{20} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (v) a carboxylic acid of formula $-(R_{21})_n$ -COOH or ester of formula $-(R_{22})$ -COO- R_{23} , where R_{21} , R_{22} , and R_{23} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (vi) halogen;
- (vii) an alcohol of formula $(R_{24})_m$ -OH or an ether of formula $-(R_{24})_n$ -O- R_{25} , where R_{24} and R_{25} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (viii) $-NR_{26}R_{27}$, where R_{26} and R_{27} are independ-25 ently selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (ix) -NHCOR₂₈, where R₂₈ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (x) $-SO2NR_{29}R_{30}$, where R_{29} and R_{30} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;

- (xi) any two of R₃, R₃, R₄, R₄, R₅, R₅, R₆, or R₆, taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;
 - (c) $R_{\text{1}},\ R_{\text{8}},\ R_{\text{9}},\ \text{and}\ R_{\text{10}}$ are independently selected from the group consisting of,
 - (i) hydrogen;
- (ii) alkyl that is optionally substituted with 10 a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (iii) five, six, eight, nine, or ten membered
 15 monocyclic or bicyclic heterocyclic ring, where the ring
 is optionally substituted with one or more halogen or
 trihalomethyl substituents;
- (iv) ketone of formula $-CO-R_{31}$, where R_{31} is selected from the group consisting of hydrogen, alkyl, or 20 a five or six membered heterocyclic ring;
- (v) a carboxylic acid of formula $-(R_{32})_n$ -COOH or ester of formula $-(R_{33})_m$ -COO- R_{34} , where R_{32} , R_{33} , and R_{34} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and 25 n and m are independently 0 or 1;
 - (vi) halogen;
- (vii) an alcohol of formula $(R_{35})_m$ -OH or an ether of formula $-(R_{35})_n$ -O- R_{36} , where R_{35} and R_{36} are independently chosen from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (viii) $-NR_{37}R_{38}$, where R_{37} and R_{38} are independently selected from the group consisting of hydrogen,

oxygen, alkyl, and a five or six membered heterocyclic ring;

- (ix) -NHCOR₃₉, where R₃₉ is selected from the group consisting of hydroxyl, alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (x) $-SO2NR_{40}R_{41}$, where R_{40} and R_{41} are selected from the group consisting of hydrogen, oxygen, alkyl, and a five or six membered heterocyclic ring;
- (xi) any two of R_1 , R_8 , R_9 , or R_{10} taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the indole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring; and
 - (d) R_{11} is hydrogen or alkyl

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- 9. An indolinone compound having a substituent at the 5 position of the oxindole ring, where the substituent at the 5 position of the oxindole ring is selected from 20 the group consisting of
 - (a) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
 - (b) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- 30 (c) a ketone of formula $-CO-R_{10}$, where R_{10} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
 - (d) a carboxylic acid of formula (R_{11}) n-COOH or ester of formula (R_{12}) –COO- R_{13} , where R_{11} , R_{12} , and R_{13}

231

and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

- (e) halogen;
- 5 (f) an alcohol of formula (R_{14}) m-OH or an ether of formula $-(R_{14})$ n-O- R_{15} , where R_{14} and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- 10 (g) $-NR_{16}R_{17}$, where R_{16} and R_{17} are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (h) -NHCOR $_{18}$, where R $_{18}$ is selected from the group consisting of alkyl, and a five or six membered 15 heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (i) $-SO2NR_{19}R_{20}$, where R_{19} and R_{20} are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- 20 (j) any two of R_4 , R_5 , R_6 , or R_7 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the oxindole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring.

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10. The compound of claim 9 of the following formula,

$$\begin{array}{c|c}
R_4 & R_7 & R_1 \\
R_5 & R_7 & R_7 \\
R_6 & R_7 & H
\end{array}$$

where (a) R_5 is selected from the group consisting of,

- (i) alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten 5 membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring
 is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (iii) a ketone of formula -CO- R_{10} , where R_{10} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
- (iv) a carboxylic acid of formula $-(R_{11})\,n$ -COOH or ester of formula $-(R_{12})\,-$ COO- R_{13} , where R_{11} , R_{12} , and R_{13} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- 20 (v) halogen;
 - (vi) an alcohol of formula (R_{14}) m-OH or an ether of formula $-(R_{14})$ n-O- R_{15} , where R_{14} and R_{15} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;

- (vii) $-NR_{16}R_{17}$, where R_{16} and R_{17} are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (viii) -NHCOR₁₈, where R_{19} is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- $(ix) \quad -SO_2NR_{19}R_{20}, \text{ where } R_{19} \text{ and } R_{20} \text{ are selected}$ from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
 - (x) any two of R_4 , R_5 , R_6 , or R_7 taken together form a bicyclic or tricyclic hetercyclic moiety fused to the six membered ring of the oxindole, where each ring in the multicyclic moiety is a five or six membered heterocyclic ring;
- (b) R_1 is selected from the group consisting of a five, six, eight, nine, and ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more substituents selected from the group consisting of
- (i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
 - (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
- 30 (iii) a ketone of formula $-CO-R_{21}$, where R_{21} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;
 - (iv) a carboxylic acid of formula (R_{22}) n-COOH or ester of formula (R_{23}) -COO- R_{24} , where R_{22} , R_{23} , and R_{24}

and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and m and n are independently 0 or 1;

- (v) halogen;
- (vi) an alcohol of formula (R_{25}) m-OH or an ether of formula $-(R_{25})$ n-O- R_{26} , where R_{25} and R_{26} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
- (viii) -NHCOR₂₉, where R₂₉ is selected from the
 group consisting of alkyl, and a five or six membered
 15 heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
 - (ix) $-SO_2NR_{30}R_{31}$, where R_{30} and R_{31} are selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (c) R_4 , R_6 , and R_7 are independently selected from the group consisting of,
- (i) hydrogen and alkyl that is optionally substituted with a monocyclic or bicyclic five, six, eight, nine, or ten membered heterocyclic ring, where the ring is optionally substituted with one or more halogen, or trihalomethyl substituents;
- (ii) five, six, eight, nine, or ten membered monocyclic or bicyclic heterocyclic ring, where the ring is optionally substituted with one or more halogen or trihalomethyl substituents;
 - (iii) a ketone of formula $-CO-R_{32}$, where R_{32} is selected from the group consisting of hydrogen, alkyl, or a five or six membered heterocyclic ring;

- (iv) a carboxylic acid of formula $-(R_{33})\,n$ -COOH or ester of formula $-(R_{34})\,-$ COO- R_{35} , where R_{33} , R_{34} , and R_{35} and are independently selected from the group consisting of alkyl or a five or six membered heterocyclic ring and 5 m and n are independently 0 or 1;
 - (v) halogen;
- (vi) an alcohol of formula (R_{36}) m-OH or an ether of formula $-(R_{36})$ n-O- R_{37} , where R_{36} and R_{37} are independently selected from the group consisting of alkyl and a five or six membered heterocyclic ring and m and n are independently 0 or 1;
 - (vii) $-NR_{38}R_{39}$, where R_{38} and R_{39} are independently selected from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring;
- (viii) $-NHCOR_{40}$, where R_{40} is selected from the group consisting of alkyl, and a five or six membered heterocyclic ring, where the ring is optionally substituted with alkyl, halogen, carboxylate, or ester;
- $(ix) \quad -SO_2NR_{41}R_{42}, \text{ where } R_{41} \text{ and } R_{42} \text{ are selected} \\$ 20 from the group consisting of hydrogen, alkyl, and a five or six membered heterocyclic ring; and
 - (d) R, is hydrogen or alkyl.
 - 11. A compound having formula XXI, wherein:

$$(OR_1)_m$$
 R_3
 R_2
 R_3
 R_4
 R_4
 R_5

XXI

- (a) A is a five or six membered ring comprised of atoms selected from the group consisting of oxygen,5 carbon, sulfer and nitrogen;
 - (b) m is zero, 1, or 2;
 - (c) R_1 is hydrogen, C_1 - C_6 alkyl or C_2 - C_6 alkanoyl;
 - (d) one of R_2 and R_3 independently is hydrogen and the other is a substituent selected from:
- 10 (1) a C_1 - C_6 alkyl group substituted by 1, 2 or 3 hydroxy groups;
 - (2) SO_3R_4 in which R_4 is hydrogen or C_1 - C_6 alkyl unsubstituted or substituted by 1, 2 or 3 hydroxy groups;
- (3) SO_2NHR_5 in which R_5 is as R_4 defined above or 15 a $-(CH_2)_n-N(C_1-C_6$ alkyl)₂ group in which n is 2 or 3;
 - (4) $COOR_6$ in which R_6 is C_1-C_6 alkyl unsubstituted or substituted by phenyl or by 1, 2 or 3 hydroxy groups or phenyl;
- (5) CONHR, in which R, is hydrogen, phenyl or C_1 -20 C_6 alkyl substituted by 1, 2 or 3 hydroxy groups or by phenyl;
 - (6) NHSO₂R₈ in which R₈ is C_1 - C_6 alkyl or phenyl unsubstituted or substituted by halogen or by C_1 - C_4 alkyl;
- (7) $N(R_9)_2$, NHR₉ or OR₉ wherein R₉ is C_2 -C₆ alkyl substituted by 1, 2 or 3 hydroxy groups;
 - (8) NHCOR $_{10}$, OOCR $_{10}$ or CH_2OOCR_{10} in which R_{10} is C_1 C_6 alkyl substituted by 1, 2 or 3 hydroxy groups;
 - $(9) \, NHCONH_2; \qquad NH-C \, (NH_2) = NH; \qquad C \, (NH_2) = NH; \\ CH_2NHC \, (NH_2) = NH; \quad CH_2NH_2; \quad OPO \, (OH)_2; \quad CH_2OPO \, (OH)_2; \quad PO \, (OH)_2; \quad or \quad a$

X N Z

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wherein X is selected from the group consisting of CH_2 , SO_2 , CO, or $NHCO(CH_2)_p$ in which p is 1,2, or 3 and Z is CH_2 ,

237

O or $N-R_{11}$ in which R_{11} is hydrogen or is as R_9 defined above.

- 12. A method of making an indolinone compound of any one of claims 5-11 comprising the steps of reaching an appropriate aldehyde and oxindol and separating the indolinone from the aldehyde and oxindol reactants.
- 13. A pharmaceutical composition comprising (i) a 10 pharmaceutically acceptable carrier or excipient and (ii) a compound according to any one of claims 5-11.
- 14. A method for treating a disease related to unregulated tyrosine kinase signal transduction, the method comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims 5-11.
- 15. A method for regulating tyrosine kinase signal 20 transduction comprising administering to a subject a therapeutically effective amount of a compound according to any one of claims 5-11.
- 16. A method of preventing or treating an abnormal condition in an organism, where the abnormal condition is associated with an aberration in a signal transduction pathway characterized by an interaction between a protein kinase and a natural binding partner, where the method comprises the following steps:
- 30 (a) administering a compound of any one of claims 5-11 to an organism; and
 - (b) promoting or disrupting the abnormal interaction.

WO 98/07695

- 17. A method of preventing or treating an abnormal condition in an organism, where the abnormal condition is associated with an aberration in a signal transduction pathway characterized by an interaction between a protein kinase and a natural binding partner, where the method comprises the following steps:
 - (a) administering a compound of any one of claims 5-11 to an organism; and
- $% \left(\frac{1}{2}\right) =0$ (b) promoting or disrupting the abnormal interaction.

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Br
$$O_2$$
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FIG. IA.

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FIG. 1B.

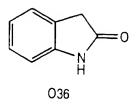
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FIG. 1C.

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Oxindole [4,5-b] pyrrole O43

Oxindole [4,5-b] pyrrole O44

Oxindole [4,5-b] pyrrole O45

FIG. IE.

FIG. IF.

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FIG. IG.

FIG. 1H.

FIG. / I.

Fig 1. Sheet 10 of 12

11/42

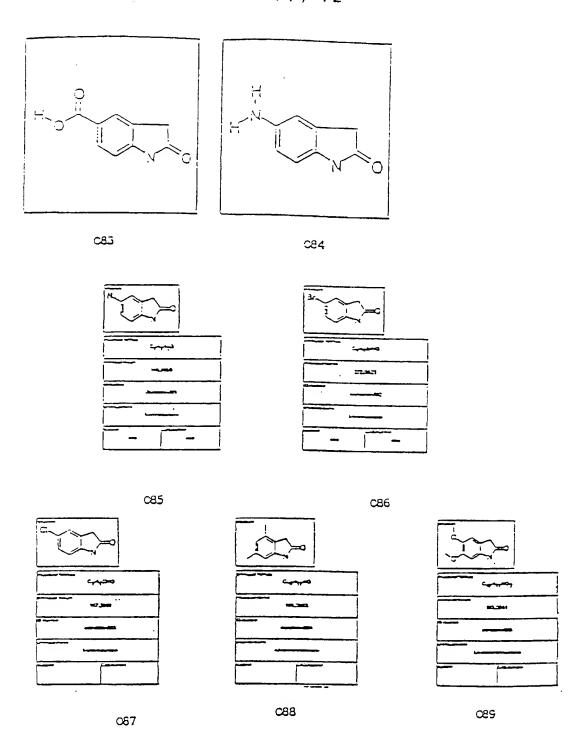


Fig 1. Sheet 11 of 12

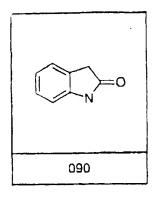


Figure 1, Sheet 12 of 12

Figure 2, Sheet 1 of 30

Figure 2, Sheet 3 of 30

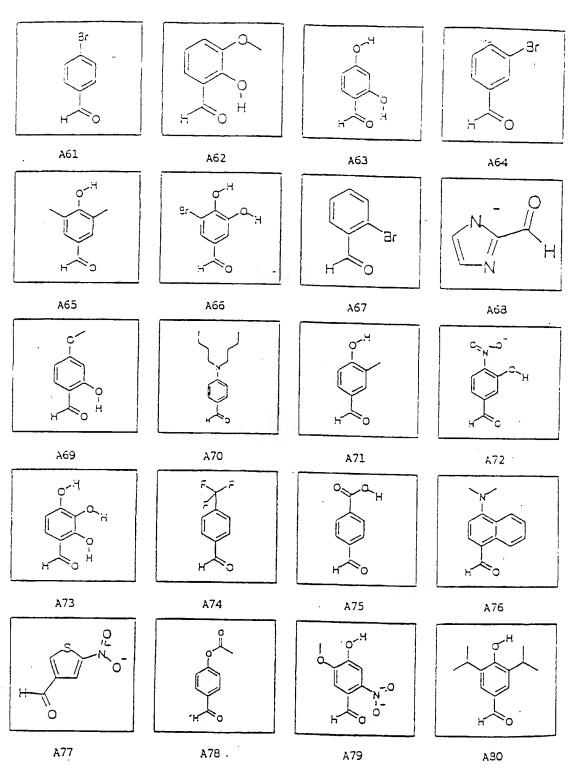


Figure 2, Sheet 4 of 30

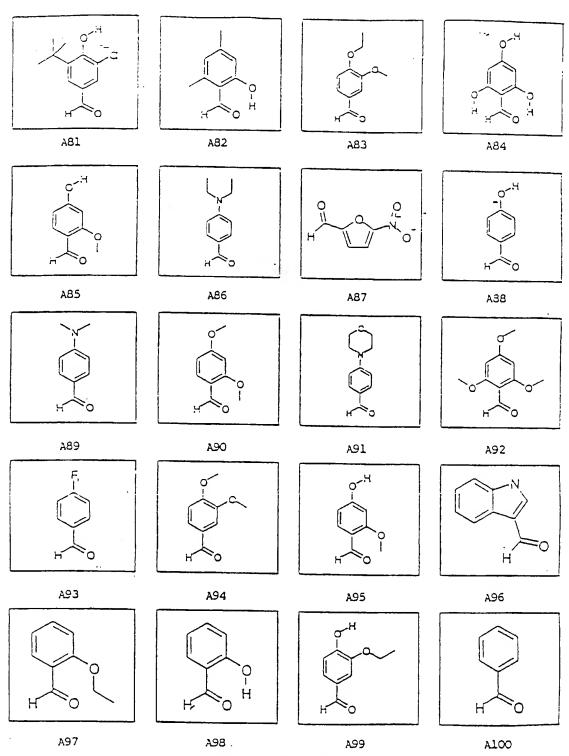


Figure 2, Sheet 5 of 30

Figure 2, Sheet 6 of 30

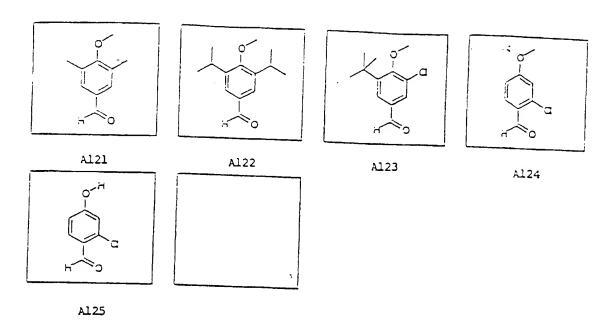
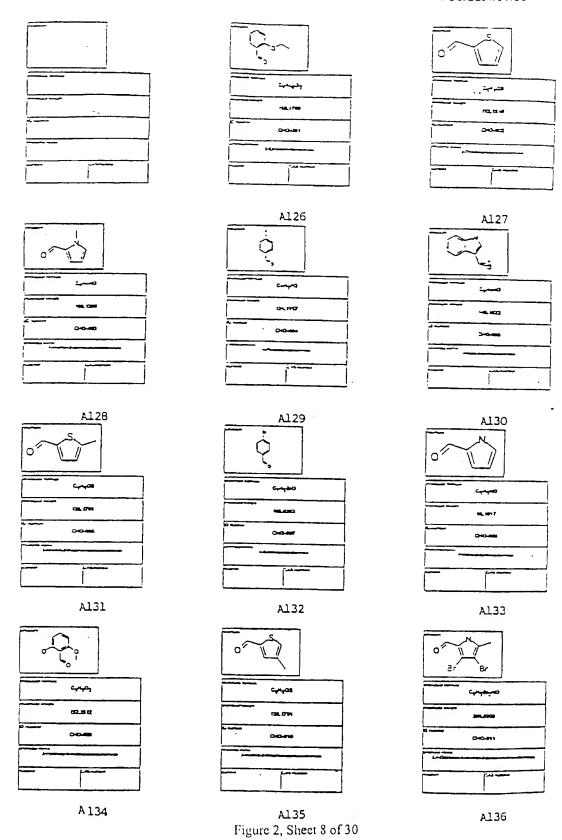
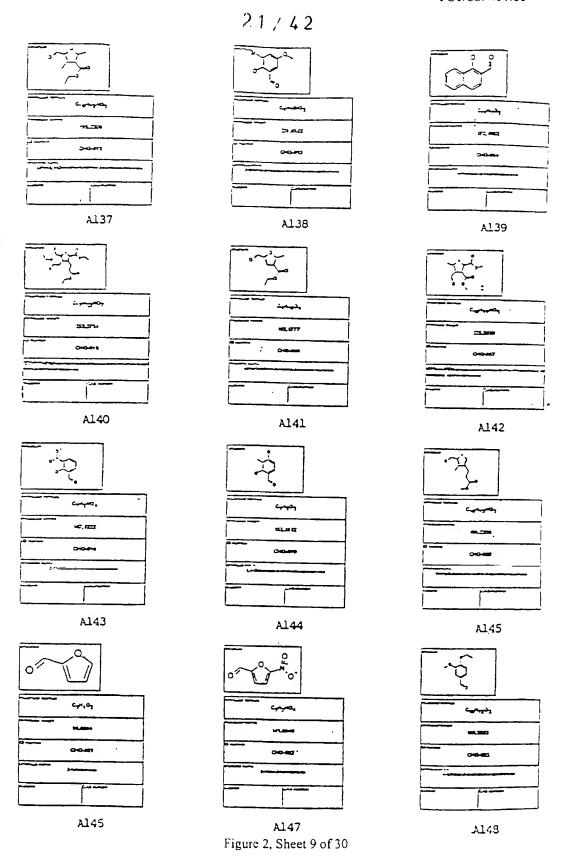
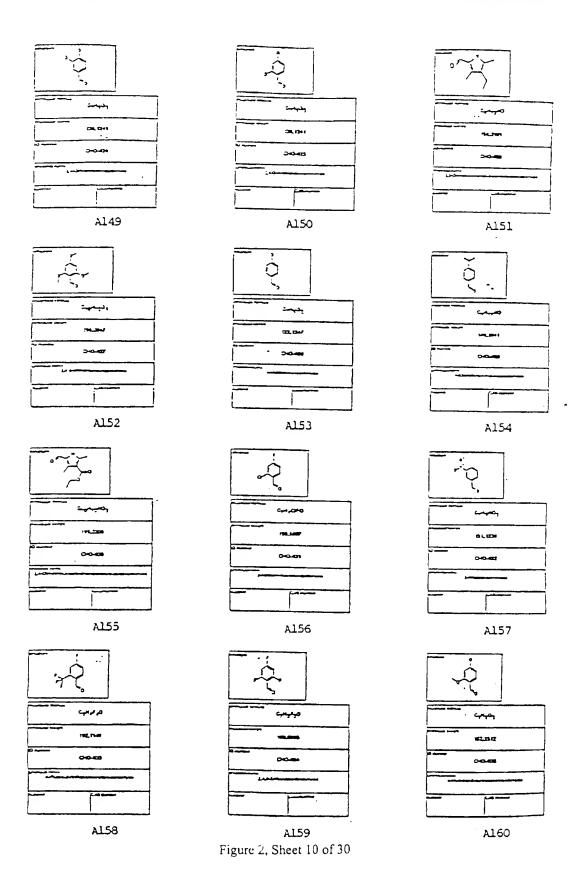
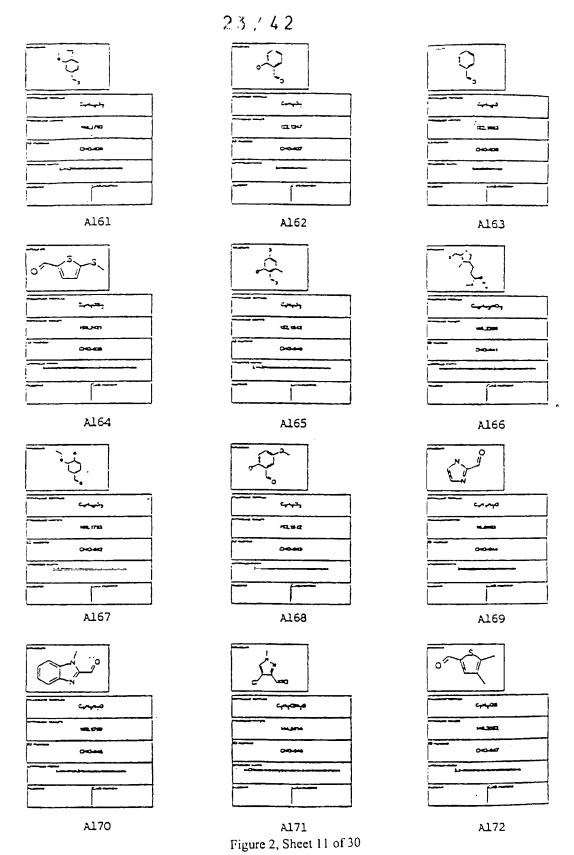


Figure 2, Sheet 7 of 30









Al83 Figure 2, Sheet 12 of 30

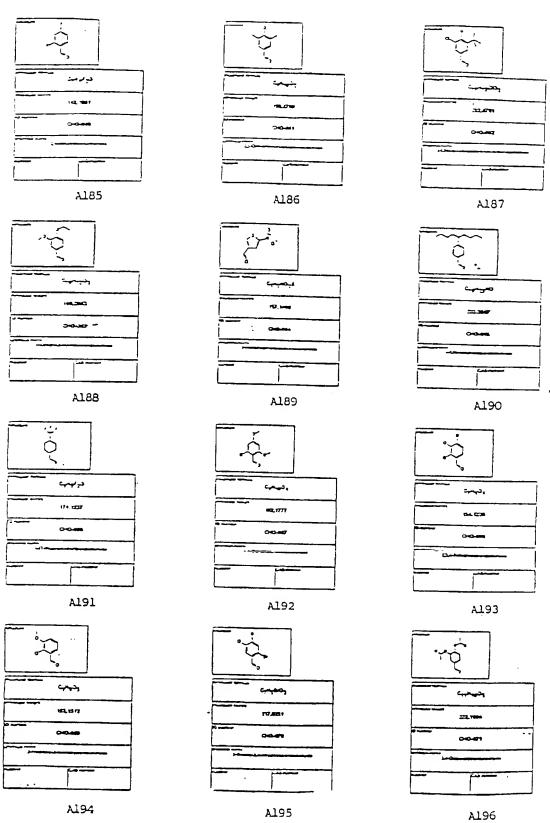


Figure 2, Sheet 13 of 30

Figure 2, Sheet 14 of 30

A208

A230 Figure 2, Sheet 16 of 30

Figure 2, Sheet 18 of 30

Figure 2, Sheet 21 of 30

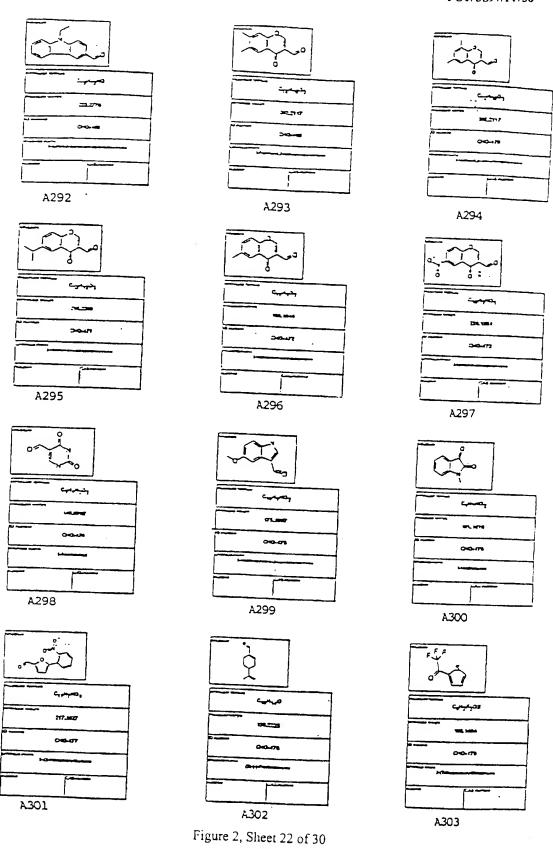


Figure 2, Sheet 23 of 30

Figure 2, Sheet 24 of 30

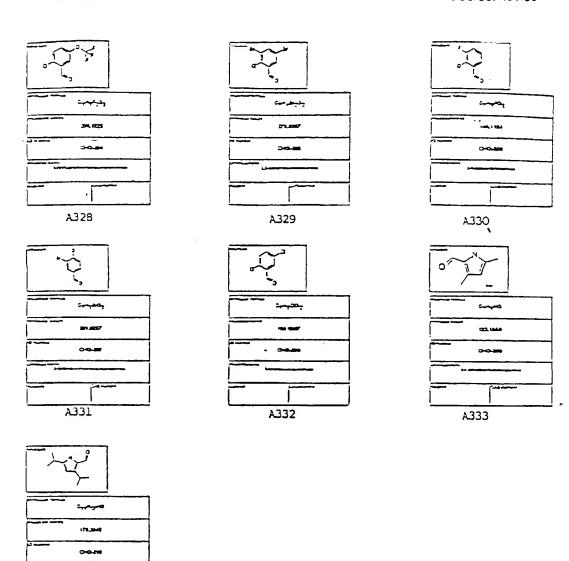


Figure 2, Sheet 25 of 30

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Figure 2, Sheet 26 of 30

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Figure 2, Sheet 28 of 30

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Figure 2, Sheet 29 of 30

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Figure 2, Sheet 30 of 30

internationa plication No PCT/US 97/14736

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According to	o International Patent Classification (IPC) or to both natio	nal classification and	IPC	
B. FIELDS	SEARCHED			
Minimum do IPC 6	cumentation searched (classification system followed b CO7D	y classification symbo	ols)	
Documentati	on searched other than minimum documentation to the	extent that such docu	iments are included in the fields	searched
Electronic da	ata base consulted during the international search (nam	e of data base and,	where practical, search terms us	ed)
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT	·		
Category *	Citation of document, with indication, where appropriat	te, of the relevant pa	ssages	Relevant to claim No
Х	EP 0 525 472 A (ERBA CARLO 1993 see the whole document	SPA) 3 Feb	pruary	5-17
X	WO 96 22976 A (PHARMACIA S FRANCO (IT); BRASCA MARIA 1 August 1996 cited in the application see claims; examples			5-17
X	WO 96 00226 A (PHARMACIA S FRANCO (IT); BRASCA GABRIE 4 January 1996 see claims; examples			5-17
X	WO 95 01349 A (ERBA CARLO 1995 see the whole document	SPA) 12 Jan	nuary	10-17
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X Furth	her documents are listed in the continuation of box C	X	Patent family members are list	ed in annex.
"A" docume consid "E" earlier of filing d "L" docume which is citation "O" docume other n "P" docume later th	nt which may throw doubts on priority claim(s) or is offed to establish the publication date of another no or other special reason (as specified) ant referring to an oral disclosure, use, exhibition or	or cu 'X' dox cu 'Y' dox dc m in '&' dox	er document published after the a principle of the principle or vention turnent of particular refevance; the funnot be considered novel or can volve an inventive step when the sument of particular relevance; the unnot be considered to involve are pourment is combined with one or ents, such combination being ob- the art.	int the application but theory underlying the eclaimed invention not be considered to document is taken alone eclaimed invention inventive step when the more other such doouvious to a person skilled out family
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Name and m	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 MV Rijswijk Tel. (+31-70) 340-2040, Tx: 31 651 epo nl. Fax: (+31-70) 340-3016	Au	De Jong, B	

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Internation. pplication No
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C.(Continue Category *	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Calegory	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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3

International application No PCT/US 97/14736

BoxI	Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons
1. X	Claims Nos because they relate to subject matter not required to be searched by this Authority, namely see FURTHER INFORMATION sheet PCT/ISA/210
2 X	Claims Nos.: because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carned out, specifically see FURTHER INFORMATION sheet PCT/ISA/210
3	Claims Nos. because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)
Box II	Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This Int	ternational Searching Authority found multiple inventions in this international application, as follows:
1 [As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3,	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos.
Rema	The additional search fees were accompanied by the applicant's protest No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 5, 9-13

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 5, 9-13 are so broad that for determining the scope of a meaningful international search due account has been taken of Rule 33.3 PCT; special emphasis was put on combinatorial libraries of indolinone compounds.

Remark: Although claims 14-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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